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Efficacy and Safety of Unani Formulation in the Management of Sayalān al-Raḥim (Leucorrhoea): A Comprehensive Prospective Clinical Study

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Abstract:

Background: Sayalān al -Raḥim (Leucorrhoea) is a common gynecological condition characterized by abnormal vaginal discharge, often associated with bacterial vaginosis, candidiasis, and altered vaginal flora. Traditional treatments may not always be effective, necessitating alternative therapeutic approaches . This study aimed to evaluate the efficacy and safety of a Unani formulation in treating Sayalān al -Raḥim (Leucorrhoea) and to assess its impact on various clinical parameters, including Pap smear results, bacterial flora composition, and vaginal pH levels. **Methods**: A randomized controlled trial with 26 patients in each group (test and control) compared the efficacy of Unani formulation versus standard treatment. Assessments included Pap smear, Gram staining, Nugent scoring, vaginal pH, and yeast cell presence in KOH preparations before and after treatment. Safety parameters like CBC, LFT, and KFT were monitored. **Results:** In the test group, the percentage of patients with normal Pap smear results increased significantly from 3.85% before treatment to 100% after treatment, while the control group saw an increase from 3.85% to 69.23%. Nugent scoring indicated a substantial shift from bacterial vaginosis to normal flora in the test group, with the proportion of patients with normal flora rising from 38.46% to 73.08% post-treatment. The control group also showed improvement, though less pronounced. Furthermore, before treatment, no participants exhibited normal pH levels. Post-treatment, 100% of the test group and 80.77% of the control group achieved normal pH levels, indicating a significant positive impact of the Unani formulation (Fisher exact test, $p = 0.05$). The presence of yeast and clue cells significantly decreased in the test group post-treatment (McNemar's test, $p < 0.0001$), demonstrating the antifungal efficacy of the formulation. All safety parameters, including CBC, LFT, and KFT, remained stable throughout the treatment period, indicating the safety of the test drug. **Conclusion:** The Unani formulation (*safuf*) demonstrated superior efficacy in treating Sayalān al -Raḥim, achieving significant improvements in Pap smear results, bacterial flora composition, and vaginal pH levels.

Keywords: Sayalān al -Raḥim, Leucorrhoea, Unani medicine, bacterial vaginosis, candidiasis, vaginal flora, Pap smear, Nugent scoring, vaginal pH, alternative therapy

Introduction

Women's health is crucial to the overall well-being of society, and gynecological morbidity is a significant concern for women in India. The range of gynecological issues extends from life-threatening cancers to conditions like Sayalān al-Raḥim (Leucorrhoea), which, while not fatal, can cause considerable psychological distress. Sayalān al-Raḥim, commonly known as leucorrhoea, is a prevalent gynecological condition characterized by an abnormal white or yellowish discharge from the female genital tract.[1] This condition, while often perceived as benign, can significantly impact the quality of life, leading to discomfort, anxiety, and in severe cases, indicative of underlying health issues. In the Unani system of medicine, an ancient holistic approach rooted in Greco-Arabic traditions, Sayalān al-Raḥim is understood through a multifaceted lens, encompassing both humoral imbalances and lifestyle factors.[2-4] Leucorrhoea is a symptom rather than a disease itself, often associated with infections, hormonal imbalances, or malignancies.

Leucorrhoea which is characterized by excessive vaginal discharge can be physiological or pathological. Physiological causes include hormonal changes during puberty, ovulation, pregnancy, and menstrual cycles, as well as stress and sexual arousal.[5,6] Pathological causes involve infections like bacterial vaginosis, Trichomonas vaginalis, and Candida, as well as foreign bodies, cervicitis, atrophic vaginitis, and STIs.[5-7]This condition, characterized by excessive vaginal discharge, accounts for over 25% of gynecologist visits, with 90% of cases attributed to Bacterial Vaginosis, Candidiasis, and Trichomoniasis.[8,9] According to the Unani concept, Leucorrhoea represents a chronic inflammation affecting the mucous membrane (Ghishā'Mukhāṭì) of the vagina. Contributing factors include Faqr alDam (anemia), Ḍu'f alBadanī (general body weakness), and Waramal-Raḥim (uterine inflammation). Ibn Sina's perspective posits a weakening of the Quwwat Hāḍima (digestive faculty) of Urūq Ḥayḍ and an imbalance in the Akhlāṭ Arba'a (four humors), resulting from Ufūnat (uterine infection), leading to Sayalan Al-Raḥim. [10]

In India, various local terms are culturally employed to describe this symptom, indicating a deep-seated concern among both genders, irrespective of the discharge being non-pathological. While there exists a considerable body of research examining genital secretions among men from anthropological, medical, and clinical perspectives, the literature pertaining to women remains relatively sparse. In North India, a multitude of local terms such as "safedpanni" (white water), "dhatu," "dholapani," "swedpradhar," and "sharer dhovay" are utilized to describe this phenomenon.[11] These terms are often accompanied by somatic manifestations including

weakness, dizziness, and a burning sensation in the hands and feet, along with significant social stress and menstrual irregularities.[11] Associations have been drawn between this condition and various psychosocial factors such as depression, verbal abuse, sexual violence, concerns regarding marital fidelity, low social integration, and diminished autonomy.[12,13] Mental tension has also been identified as a causative factor in Ayurvedic literature.[14] Women attribute the onset of vaginal discharge to environmental factors, dietary habits, weakness, and tension, while biomedical factors such as unsafe delivery, copper-T insertion, abortion, and multiple partners have also been implicated.[15,16]

Conventional treatments typically involve antibiotics or hormone therapies, which, while effective, can have side effects and may not address the root cause of the imbalance. Therefore, there is a growing interest in alternative and complementary therapies, particularly those that offer holistic and natural remedies. Unani medicine offers a comprehensive approach to the management of Sayalān al -Raḥim, emphasizing the restoration of humoral balance, lifestyle modifications, and the use of natural formulations. Unani practitioners have developed specific formulations believed to rectify the underlying humoral disturbances, improve general health, and provide symptomatic relief. These formulations often include a combination of herbs and natural substances, chosen for their purported efficacy in treating gynecological issues. This study aims to explore the therapeutic potential of a specific Unani formulation in the management of Sayalān al -Raḥim. By evaluating its efficacy and safety, this research seeks to provide a scientific basis for the use of traditional Unani treatments in modern gynecological practice. The study will involve a detailed assessment of the formulation's impact on the symptoms of leucorrhoea, overall patient well-being, and any observed side effects.

Material and methods

The present study was conducted at the Department of Mo'alajat, Regional Research Institute of Unani Medicine (RRIUM), Srinagar, University of Kashmir. Approved by the Institutional Ethics Committee (IEC No. RRIUM-SGR/MD-2021/CT/SAR/LUF) and registered in the Clinical Trials Registry of India (CTRI No. CTRI/2023/03/050719), the study began in May 2023. Patients were enrolled from the OPD of RRIUM hospital and the Department of Gynecology at SDH Habak. Out of 93 patients screened, 35 were excluded for not meeting inclusion criteria, and 6 dropped out. Ultimately, 52 patients completed the trial. The study was a randomized, single-blind, standard-controlled trial conducted over one year. The sample size included 52 patients, with 26 in the test group and 26 in the control group. Before starting the experiment, a protocol was reviewed and approved by the Institutional Ethics Committee of

RRIUM, Srinagar. The clinical study commenced following ethical approval, with data collected through history taking, clinical (PS and PV) and microscopic examination, and screening.

Patients were enrolled in the study based on the following criteria:

Inclusion Criteria: Married women aged 18-45 years exhibiting symptoms of leucorrhoea, such as excessive white discharge, lower back pain, lower abdominal pain, dyspareunia, and dysuria. Patients diagnosed with bacterial vaginosis, trichomonas infection, and vaginal candidiasis through wet mount tests, AMSEL criteria, and Nugent's scoring.

Exclusion Criteria: Pregnant and lactating mothers, patients with chronic PID, those under 18 or over 45 years of age, patients with systemic illnesses (hypertension, malignancies, diabetes, cardiovascular disease, CKD, CLD), patients with hypersensitivity to the control drug combination (secnidazole, fluconazole, and azithromycin), and patients who are HIV, HBsAg, or HCV positive.

Patients meeting the aforementioned inclusion criteria were provided with a patient information sheet detailing the study's nature and treatment methods. They were given ample time to review its contents and raise any queries. Upon agreement to participate, informed consent was obtained through signature. Only patients meeting all inclusion criteria were enrolled in the study and randomized into test or control groups using computer-based randomization.

Subsequently, patients underwent a comprehensive history and physical examination, including pelvic examination. Details regarding the emergence and characteristics of current clinical symptoms, such as vaginal discharge, were documented. Patients were queried about associated symptoms and past medical history, including pelvic inflammation disease and venereal illnesses, along with menstrual and obstetric history. Additionally, sexual activity frequency, contraception use, and pharmacological history were assessed. Verbal consent was obtained prior to examinations and sampling. Diagnostic investigations for bacterial vaginosis, vaginal candidiasis, and trichomoniasis were conducted to ensure eligibility. Patient history, clinical symptoms, and investigation results were recorded on a designated case report form (CRF). Necessary tests including wet mount tests, gram staining, pap smear, USG pelvis, RBS, and urine (routine) were conducted, along with CBC, LFT, KFT, and triple serology for sexually transmitted diseases. Thorough history-taking and physical examination, including vital signs monitoring and systemic examination, were performed and recorded in the CRF. A detailed gynecological history and pelvic examination were conducted with verbal consent. Socioeconomic status was also assessed based on educational background, occupation, and monthly income.

Diagnostic Evaluation

Gynecological Examination: Verbal consent was obtained from each patient for specimen collection and vaginal examination. Patients were instructed to urinate prior to the examination and positioned in a dorsal position with knees flexed for local assessment. The perineum was inspected for abnormalities, and the vulva was examined for erythema, rashes, excoriations, and irritation. Patients were then asked to cough or strain to check for associated prolapse.

Measurement of Vaginal Discharge pH: The pH of the vaginal discharge was measured by cleaning the lower vagina with a sterile swab and using Ranbaxy pH indicator paper, which has a color range of 4 to 7. To avoid cervical mucus contamination, the paper was placed on the anterior vaginal fornix, removed, and compared to the supplied color scale. A pH between 4 and 4.5 suggested candidiasis, while a pH greater than 5 indicated bacterial vaginosis or trichomoniasis, in conjunction with other diagnostic criteria.

Per Speculum Examination: A Cusco's speculum examination was conducted under appropriate illumination. The quantity, color, consistency, and odor of the discharge were observed, and the condition of the cervix and vagina was noted. Any abnormalities, such as inflammation or a strawberry appearance of the cervix, were recorded. Discharge samples were collected on a cotton swab to determine color.

Sampling Technique: A sterile swab was inserted into the posterior vaginal fornix under aseptic conditions, and smears were prepared on four glass slides. Two slides were heat-fixed for Gram staining, and two were used for the Whiff test. A bimanual examination was performed to assess the size, position, mobility, and condition of the uterus and adnexa. Any mass or tenderness in the fornices and pouch of Douglas was noted. Smears were immediately examined microscopically at 10x10 and 10x40 magnifications. The first slide, made with normal saline, was checked for epithelial cells, clue cells, Trichomonas vaginalis, and pus cells. The second slide, prepared with 10% KOH solution, was examined for WBCs, bacteria, epithelial cells, and yeast. The time between specimen collection and microscopic analysis was limited to 15 minutes.

Whiff Test: Following the speculum examination, three drops of 10% KOH were added to the swab or discharge on the speculum. A positive Whiff test was indicated by a fishy odor.

Gram Staining: A swab from the lateral vaginal wall was rolled on two glass slides. The first smear was heat-fixed and Gram-stained using safranin as the counterstain. Morphotypes observed under oil immersion (1000x magnification) included large Gram-positive rods (Lactobacillus), small Gram-variable rods (Gardnerella vaginalis), small Gram-negative rods

(Bacteroides species), curved Gram-variable rods (Mobiluncus species), and Gram-positive cocci. The second slide was Giemsa-stained and examined for epithelial cell abnormalities and pathological microflora.

Bimanual Examination: After the speculum examination, a manual vaginal examination was performed to evaluate the size, location, mobility, and condition of the uterus and adnexa. Any mass or tenderness in Douglas' pouch was recorded.

Pap smear: Pap smear test was also Pap smear was also performed to screen for cervical abnormalities and infections.

Clinical Diagnosis:

Bacterial Vaginosis: Diagnosed based on Amsel's criteria and Nugent's scoring, requiring any three of the following: thin white-grey discharge, vaginal pH >4.5, fishy odor on adding KOH (Whiff test), and presence of clue cells on microscopy.

Candidal Vaginitis: Diagnosed by thick, curdy discharge, vaginal pH 4-4.5, absence of odor, and presence of yeasts or pseudohyphae on KOH mount.

Trichomoniasis: Diagnosed by vaginal pH >5.5, thin greenish discharge with inflammation, strawberry cervix, and direct observation of the organism in a wet mount.

Diagnosed patients with bacterial vaginosis, candidiasis, and trichomoniasis were enrolled in the clinical trial after providing written consent. Participants were randomly assigned to test and control groups using computer-based randomization. The test group, comprising 26 patients, received the test drug Safūf at a dosage of 10 grams twice daily for 21 days. The control group, also consisting of 26 patients, received the standard drug Zocoon kit (a combination of Secnidazole 2g, Fluconazole 150 mg, and Azithromycin 1g as a single dose).

Criteria for Selection of Drugs

The treatment regimen for this condition necessitates drugs with astringent, styptic, desiccant, blood-purifying, anti-inflammatory, antibacterial, and antifungal properties. A compound formulation including Taj (Cinnamomum cassia), Majeet (Rubia cordifolia), Samag-e-Dhak (Butea monosperma), Gokru (Tribulus terrestris), and Gul-e-Pista (Pistacia vera) was selected based on these criteria after a thorough review of Unani literature. The highest quality drugs were sourced from the Regional Research Institute of Unani Medicine, Srinagar. Each ingredient was authenticated prior to preparation. The herbs were mixed in equal quantities with 50 kg of sugar, ground to a fine powder (Safūf), and sieved through Sieve No. 100. The formulation was dispensed in 140-gram airtight jars, with a daily dosage of 10 grams twice daily taken with milk.

Treatment efficacy

The evaluation of treatment effectiveness was conducted through a thorough examination of various objective parameters. These included the pH level of vaginal discharge, the results of the Whiff test (also known as the Amine test), Gram staining analysis of vaginal discharge, examination of wet mounts, KOH mounts, and Pap smear tests. Each of these assessments played a crucial role in determining the response and efficacy of the treatment regimen.

This structured approach ensures a comprehensive evaluation of the therapeutic efficacy and safety of the Unani formulation in managing leucorrhoea.

Results

In the present study , we noted that among the 52 patients diagnosed with Sayalān al - Raḥim, a predominant proportion (34.62%) fell within the age range of 39-45 years, with nine patients each in the test and control. Subsequently, 61.54% were distributed across the 25-31 years (test: 8, control: 8) and 32-38 years (test:9, control: 7). Additionally, a minority (3.85%) of patients, specifically two individuals from the control group, were categorized within the 18-24 years age category. The test group had a mean age of 39.34 ± 2.166 years, and the control group had a mean age of 40.31 ± 2.366 years, with no significant age difference ($p = 0.128$). Most of the test group patients were housewives (57.69%), followed by government employees (30.77%) and students (11.54%). The control group had 80.77% housewives and 19.23% government employees, with no students ($p = 0.09$). The predominant temperament was Balghami in both groups (test: 73.08%, control: 80.77%) with no significant difference ($p = 0.743$). The commonest socioeconomic status were "Upper Lower" (51.92%) and "Lower Middle" (38.46%). In the test group, "Upper Lower" was 53.85% and "Lower Middle" was 34.62%, while in the control group, they were 50% and 42.31%, respectively. The difference between the groups was not significant ($p = 0.452$).

The congruence in demographic parameters, signifies the effectiveness of randomization in achieving balanced representation across the test and control cohorts. This similarity in demographic profiles assures that any observed differences in objective parameters will likely be attributable solely to the administered drug interventions, rather than demographic disparities.

Table 1: Showing severity of vaginal discharge before and after the treatment in test and control group

Severity of vaginal discharge	Test				Control			
	BT		**AT**		**BT**		**AT**	
	No.	%age	No.	%age	No.	%age	No.	%age
No discharge	0	0.00	16	61.54	0	0.00	14	53.85

Mild discharge	0	0.00	10	38.46	0	0.00	11	42.31
Moderate discharge	5	19.23	0	0.00	3	11.54	1	3.85
Severe discharge	21	80.77	0	0.00	23	88.46	0	0.00
Total	26.00	100.00	26.00	100.00	26.00	100.00	26.00	100.00
Median (min,max)	3(2,3)		0(0,1)		3(2,3)		0(0,2)	
Within groups	Wilcoxon matched pair test, p-value<0.0001				Wilcoxon matched pair test, p-value<0.0001			
Test vs .Control	BT vs BT	Fisher's exact test : Exact p-value=0.703						
	AT vs AT	Chisq=2.082, df=3; p-value=0.556						

At baseline, the majority of patients in both the test and control groups exhibited severe vaginal discharge (test: 80.77%, control: 88.46%), followed by moderate vaginal discharge (test: 19.23%, control 11.53%. Importantly, both groups demonstrated comparability in the severity of the disease at baseline, as indicated by the p-value 0.776. When the treatment was administered in test and control group, we found that in the test group, the proportion of patients with no discharge increased from 0.00% to 61.54%, with a corresponding decrease in moderate (19.23%) and severe (80.77%) discharges to 0.00% post-treatment. The median severity score dropped from 3 (severe) to 0 (none), with a range narrowing from 2-3 to 0-1, indicating a substantial reduction in severity (Wilcoxon matched pair test; $p < 0.0001$). Similarly, in the control group, patients with no discharge increased from 0.00% to 56.00%, with moderate and severe discharges reducing to 3.85% post-treatment. The median severity score also decreased from 3 to 0, with the range narrowing from 2-3 to 0-2 (Wilcoxon matched pair test; $p < 0.0001$). Chi-square test comparing severity levels post treatment between the groups revealed a p-value of 0.703, indicating comparable outcomes. These findings suggest that although the proportion of patients with improvement to normal vaginal discharge post treatment was higher in test group compared to control group (61.54% vs. 53.85%) but statistically the effectiveness of the treatment in both the groups was comparable. The effectiveness of test drug in contrast to standard drug was further evaluated on assessing the improvement in objective parameters:

Table 2: Impact of Treatment on Gram Staining Patterns and Bacterial Flora Composition in Test and Control Groups

Gram staining	Test				Control			
	BT		**AT**		**BT**		**AT**	
	No.	%age	No.	%age	No.	%age	No.	%age
Normal	1	3.85	19	73.08	1	3.85	16	61.54
Intermediate	9	34.62	7	26.92	5	19.23	4	15.38
Bacterial vaginosis	16	61.54	0	0.00	20	76.92	6	23.08
Total	26	100.00	26	100.00	26	100.00	26	100.00

Mean±SD	7.01±2.98	2.44±1.23	7.55±.3.01	3.65±1.11
Within group comparison	Paired t-test;p-value<0.0001		Paired t-test;p-value<0.0001	
Test vs Control (BT vs. BT)	Independent t-test; t=-0.65, df=50; P-value=0.5186			
Test vs Control (AT vs. AT)	Independent t-test; t=-3.7, df=50; P-value<0.0001			

The evaluation of Gram staining patterns and Nugent scoring in both test and control groups pre- and post-treatment revealed significant insights into the intervention's impact on bacterial flora composition. In the test group, a notable improvement was observed, with a shift from predominantly bacterial vaginosis (61.54%) to normal flora (73.08%) post-treatment, accompanied by a decrease in the intermediate category (34.62% to 26.92%) (Paired t-test; $p < 0.0001$). Similarly, the control group exhibited significant improvement, with an increase in normal flora (3.85% to 61.54%) and reduction in bacterial vaginosis (76.92% to 23.08%) (Paired t-test; $p < 0.0001$). Mean Nugent scores decreased substantially in both groups post-treatment, indicating improved bacterial flora composition. While baseline characteristics were comparable between groups (Independent t-test; $p = 0.5186$), post-treatment analysis revealed a significant difference (Independent t-test; $p < 0.0001$), favoring the test drug. This underscores the test drug's superior efficacy in inducing positive alterations in bacterial flora composition, as evidenced by lower Nugent scores post-treatment.

Table 3: Effect of Treatments on Vaginal pH and Distribution of pH-Associated Conditions in Test and Control Groups

Vaginal pH	**Within group**				**Control**			
	BT		**AT**		**BT**		**AT**	
	No.	**%age**	**No.**	**%age**	**No.**	**%age**	**No.**	**%age**
Normal	0	0.00	26	100.00	0	0.00	21	80.77
Candidiasis (pH<4.5)	4	15.38	0	0.00	1	3.85	1	3.85
Bacterial Vaginosis (pH>4.5)	22	84.62	0	0.00	25	96.15	4	15.38
Trichomoniasis (pH>5.5)	0	0.00	0	0.00	0	0.00	0	0.00
Total	26	100.00	26	100.00	26	100.00	26	100.00
Within group comparison	Wilcoxon matched pair test, p-value<0.0001				Wilcoxon matched pair test, p-value<0.0001			
Test vs Control (BT vs. BT)	Fisher's Exact test; P-value=0.34							
Test vs Control (AT vs. AT)	Fisher's Exact test; P-value=0.05							

The thorough examination of treatment effects on vaginal pH and associated conditions in both test and control groups has provided insightful findings. In the test group, a significant shift in vaginal pH distribution was observed post-treatment, with all participants achieving a normal pH level compared to none before treatment. Bacterial vaginosis incidence decreased

from 84.62% to 0.00% after treatment (Wilcoxon matched pair test; $p < 0.0001$), with no trichomoniasis cases detected. Similarly, the control group exhibited a positive trend, with 80.77% attaining normal pH levels post-treatment ($p < 0.0001$) and a reduction in bacterial vaginosis prevalence from 96.15% to 15.38% ($p < 0.0001$), and no trichomoniasis cases. Before treatment, no significant differences in pH-associated conditions were observed between the test and control groups (Fisher's Exact test; $p = 0.34$), but a borderline divergence emerged post-treatment ($p = 0.05$). The transition to normal pH in 100% of the test group compared to 80.77% in the control group highlights the superior efficacy of the test treatment in addressing bacterial vaginosis and restoring pH balance, indicating a significant difference in treatment effectiveness.

Table 4: Comparison of Pap Smear Results Before and After Treatment in Test and Control Groups

Pap smear	Test				Control			
	BT		AT		BT		AT	
	No.	%age	No.	%age	No.	%age	No.	%age
Normal	1	3.85	26	100.00	1	3.85	18	69.23
Abnormal	25	96.15	0	0.00	25	96.15	8	30.77
Total	26	100.00	26	100.00	26	100.00	26	100.00
Within group comparison	McNemar's test;p-value<0.0001				McNemar's test;p-value<0.0001			
Test vs Control (BT vs. BT)	Fisher's Exact test; P-value=1							
Test vs Control (AT vs. AT)	Fisher's Exact test; P-value=0.004							

The analysis of Pap smear results within the test and control groups, pre- and post-treatment, revealed significant and clinically meaningful patterns. In the test group, a notable improvement was observed, with the percentage of patients exhibiting normal Pap smear results increasing from 3.85% pre-treatment to 100.00% post-treatment. Conversely, the proportion of patients with abnormal results decreased from 96.15% to 0.00% post-treatment, indicating a highly significant improvement (McNemar's test; $p < 0.0001$). Similarly, in the control group, there was a positive trend, with the percentage of patients with normal Pap smear results increasing from 3.85% to 69.23% post-treatment, and the proportion of patients with abnormal results decreasing from 96.15% to 30.77% post-treatment (McNemar's test; $p < 0.0001$). Comparative analysis between the groups revealed no substantial differences in Pap smear results pre-treatment (Fisher's Exact test; $p = 1$), but a significant differentiation emerged post-treatment (Fisher's Exact test; $p = 0.004$). This highlights the remarkable effectiveness of the test drug in improving Pap smear outcomes, establishing a statistically significant difference between the test and control groups post-treatment.

Table 5: Showing distribution of patients as presence or absence of yeast (KoH) before and after the treatment in test and control group								
Yeast cells (KoH)	Test				Control			
	BT		**AT**		**BT**		**AT**	
	No.	%age	No.	%age	No.	%age	No.	%age
Absent	20	76.92	24	92.31	18	69.23	25	96.15
Present	6	23.08	2	7.69	8	30.77	1	3.85
Total	26	100.00	26	100.00	26	100.00	26	100.00
Within group comparison	McNemar's test;p-value<0.0001				McNemar's test;p-value<0.0001			
Test vs Control (BT vs. BT)	Fisher's Exact test; P-value=0.755							
Test vs Control (AT vs. AT)	Fisher's Exact test; P-value=1							

The assessment of patients based on the presence or absence of yeast cells in potassium hydroxide (KOH) preparations before and after treatment reveals notable observations within the test and control groups. Initially, in the test group, 76.92% of patients showed the absence of yeast cells, while 23.08% had their presence. Post-treatment, a significant improvement was observed, with 92.31% displaying the absence of yeast cells and only 7.69% retaining their presence (McNemar's test; $p < 0.0001$). Similarly, in the control group, 69.23% initially lacked yeast cells, while 30.77% had their presence. Following treatment, a marked enhancement was noted, with 96.15% showcasing the absence of yeast cells and only 3.85% maintaining their presence (McNemar's test; $p < 0.0001$). Before treatment, Fisher's Exact test revealed a non-significant p-value of 0.755, indicating similar distributions of yeast cells between the test and control groups. Post-treatment, Fisher's Exact test generated a p-value of 1, suggesting comparable distributions of yeast cells between both groups. The uniformity in yeast cell distributions post-treatment underscores the consistency in treatment effects and outcomes across both groups, reinforcing the reliability and effectiveness of the treatment regimen in inducing positive changes.

Table 6: Showing distribution of patients as per clue cell (wet mount) before and after the treatment in test and control group								
Clue cells (Wet mount)	Test				Control			
	BT		**AT**		**BT**		**AT**	
	No.	%age	No.	%age	No.	%age	No.	%age
Absent	0	0.00	26	100.00	0	0.00	19	73.08
Present	26	100.00	0	0.00	26	100.00	7	26.92
Total	26	100.00	26	100.00	26	100.00	26	100.00

Within group comparison	McNemar's test;p-value<0.0001	McNemar's test;p-value<0.0001
Test vs Control (BT vs. BT)	No test applied	
Test vs Control (AT vs. AT)	Fisher's Exact test; P-value=0.010	

The evaluation of patients based on the presence or absence of clue cells in wet mount examinations before and after treatment revealed significant observations in both the test and control groups. Initially, in the test group before treatment (BT), 100% of patients exhibited the presence of clue cells. However, after treatment (AT), a notable improvement was observed, with all patients transitioning to the absence of clue cells. Similarly, in the control group BT, all patients displayed clue cells, but following AT, 73.08% showed the absence of clue cells, while 26.92% retained their presence. McNemar's test within both groups revealed highly significant p-values (<0.0001), indicating significant changes in clue cell distribution pre- and post-treatment. Comparing the groups BT revealed comparable distributions of clue cells. However, AT, Fisher's Exact test showed a significant difference (p-value=0.010) between the groups, emphasizing the effectiveness of the intervention, particularly in the test group, in inducing substantial improvements.

Discussion

This study aimed to evaluate the clinical efficacy of a test drug compared to a standard control drug in treating patients with Sayalān al -Raḥim, a condition characterized by abnormal vaginal discharge. Our findings demonstrate significant and clinically meaningful improvements in both treatment groups, with the test drug showing superior outcomes in several parameters. The randomization process was effective, as evidenced by the comparable demographic parameters between the test and control groups. The mean ages were similar (test: 39.34 years, control: 40.31 years), and there were no significant differences in the distribution of patients by age, socioeconomic status, or severity of vaginal discharge at baseline. This ensured that any observed differences in treatment outcomes could be attributed to the efficacy of the interventions rather than demographic variations.

In the present study, we observed that both the test and control groups exhibited significant improvements in the severity of vaginal discharge post-treatment. The test group showed a remarkable increase in patients with no discharge (61.54% post-treatment), while the control group also demonstrated substantial improvement (53.53% post-treatment). The median severity scores decreased significantly in both groups, indicating effective reduction in discharge

severity. The statistical analyses confirmed these improvements with highly significant p-values (<0.0001). These findings indicate that the Unani compound formulation (safuf) significantly reduces vaginal discharge, as documented in classical Unani texts such as Qaraba -ud-din Qadri, Bayaz Kabeer, and Akseer-e-Azam, where this formulation is recommended for treating Sayalān al-Raḥim (Leucorrhoea). The improvement in excessive vaginal discharge can be attributed to the pharmacological properties of the ingredients in the Unani formulation . These properties include Qābiḍ (astringent), Mujaffif (desiccant), Muḥallil (resolvent), and Dāfi‘-i-Ta‘affun (antiseptic), as described by Unani scholars. Sayalān al-Raḥim (Leucorrhoea) is primarily caused by Ḍu‘f-i Quwwatt Ghādhiya of Raḥim (weakness of the nutritive faculty of the uterus). The Mizāj (temperament) of the test drug is Bārid Yābis (cold and dry), which strengthens the uterus. Various studies have demonstrated the anti-inflammatory, antimicrobial, antifungal, and antioxidant activities of this compound formulation, which our study corroborates through phytochemical analysis.[17-19] The formulation contains tannins and flavonoids, which exhibit scavenging properties, as evidenced by phytochemical and antioxidant studies. These bioactive compounds contribute to the therapeutic efficacy observed in the reduction of vaginal discharge, supporting the traditional use of this Unani formulation in managing Sayalān al-Raḥim.

In the test group before treatment (BT), 3.85% of patients tested negative for the Whiff test, while 96.15% tested positive. Following treatment (AT), a remarkable improvement was observed, with 96.15% of patients testing negative and only 3.85% testing positive. Similarly, in the control group before treatment (BT), 3.85% of patients tested negative, and 96.15% tested positive for the Whiff test. After treatment (AT) in the control group, 69.23% of patients tested negative, and 30.77% tested positive. McNemar's test was applied to assess the changes in the distribution of Whiff test results before and after treatment within each group, revealing significant improvements in the test group compared to the control group. These findings support the efficacy of the test drug in improving Whiff test results, as compared to the control group. The results are consistent with the studies by Shroff S et al. and Gupta N et al.[20,21] The pharmacopoeial formulation proved effective in the syndromic management of abnormal vaginal discharge (AVD), improving the Whiff test outcomes due to its antimicrobial, antiseptic, and antioxidant properties. These pharmacological effects are attributed to the presence of phytoconstituents such as tannins, alkaloids, flavonoids, and polyphenolic compounds.

Diagnosis and evaluation of candidal and trichomonal vaginitis involved the examination of fungal mycelia and trichomonas presence in KOH Mount and wet mount specimens under microscopic observation, alongside gram staining to confirm the presence of these pathogens.

Assessment of cure was based on the disappearance of fungal mycelia and trichomonas, indicating successful treatment outcomes. The presence of yeast cells in KOH preparations significantly decreased in both groups after treatment. The test group saw a reduction from 23.08% to 7.69% (p-vale<0.0001), while the control group exhibited a decrease from 30.77% to 3.85% (p-value<0.0001). These changes were statistically significant, indicating effective antifungal activity of both treatment regimens. This underscores the intervention's beneficial effect in reducing yeast cell presence in the test group compared to the control group, thereby reinforcing the reliability and efficacy of the treatment regimen in eliciting positive changes in the studied parameter. The effectiveness of the test drug can be attributed to its antifungal properties, likely stemming from the presence of saponins. Notably, the triterpenoid saponin Anagallisin C, featuring an oleanolic acid aglycone, emerged as the most potent compound against C. albicans with an MIC of 1 μg/mL. Additionally, two steroidal saponins, TG-I from Trillium grandiflorum and TTS-12 from Tribulus terrestris, exhibited significant fungistatic activities against C. albicans. Studies by Nader et al., Mandalari et al., and Merghache D et al. have corroborated the antifungal properties of components such as Cinnamom cassia, Pistachia vera, and Tribulus terrestris. Moreover, the compound formulation also contains alkaloids and flavonoids, which are known to possess antifungal activities. [22-24]The evaluation of patients based on the presence or absence of clue cells in wet mount examinations before and after treatment revealed significant observations in both the test and control groups. The assessment of clue cells in wet mount examinations showed that all patients in the test group transitioned from having clue cells to none post-treatment (p-value<0.0001). In the control group, 73.08% of patients showed no clue cells after treatment (p-value<0.0001). The significant reduction in clue cells post-treatment further validates the efficacy of both interventions, with the test drug demonstrating superior performance. This coincides with the study done by AL- Dammy et al.who reported that the efficacy of test drug may be due to anti-microbial and anti-oxidant properties.[25] The antimicrobial activity observed in various extracts, particularly against gram-positive and gram-negative organisms, aligns with the findings of Siva Rama et al., who studied individual ingredients such as *Rubia cordifolia* and *Tribulus terrestris*. The antibacterial properties of these extracts are attributed to the presence of anthraquinones and terpenoids, as identified in phytochemical analyses.[26] Additionally, the antioxidant properties of the compound formulation have demonstrated significant scavenging activity, further corroborating its therapeutic efficacy.

The analysis of Gram staining patterns and Nugent scores revealed substantial improvements in bacterial flora composition in both groups. In the test group, a substantial improvement was observed, as the prevalence of bacterial vaginosis decreased from 61.54% before treatment to a majority of normal flora at 73.08% after treatment (p-value<0.0001). Similarly, the control group also demonstrated a notable enhancement in Gram staining patterns, with the percentage of patients exhibiting normal flora increasing from 3.85% before treatment to 61.54% after treatment (p-value<0.0001). The test group showed a significant shift from bacterial vaginosis to normal flora , with corresponding reductions in Nugent scores. Although the control group also improved, the test group demonstrated a more pronounced positive shift, underscoring the test drug's greater impact on bacterial flora composition. These findings robustly support the efficacy of the test drug in fostering a favorable alteration in bacterial flora composition, as evidenced by Nugent scoring. The lower Nugent scores observed in the test group post-treatment signify a more favorable and improved bacterial flora composition, highlighting the therapeutic superiority of the test drug over the control drug in alignment with the findings of Ezeigwe CO et al.[27]This study marks the first investigation into the effects of the Unani formulation on Pap smear results, thus offering novel insights not previously explored in the literature. Pap smear examinations were conducted initially to rule out any underlying clinical pathology. Surprisingly, 47 cases tested positive for BV, while 5 cases showed signs of vaginal candidiasis, with no instances of trichomoniasis detected. In the test group, a significant improvement was noted, with normal Pap smear results increasing from 3.85% to 100.00% post-treatment, alongside a decrease in abnormal results (McNemar's test; p-value < 0.0001). Similar positive trends were observed in the control group (McNemar's test; p-value < 0.0001). These findings, consistent with Gram staining results and no additional pathologies, suggest the Unani formulation's efficacy, possibly due to its antioxidant and antimicrobial properties.

pH serves as a crucial indicator of vaginal health, with deviations from the normal acidic range often indicating underlying microbial imbalances or infections. In our study, the evaluation of pH levels before and after treatment revealed significant trends within both the test and control groups. In test group; before treatment (BT), none of the participants exhibited a normal pH level, but post-treatment (AT), each individual achieved a normal pH level, reflecting a remarkable improvement. Additionally, the incidence of bacterial vaginosis (pH > 4.5) substantially decreased from 84.62% before treatment to 0.00% after treatment, as confirmed by the Wilcoxon matched pair test (p-value < 0.0001). Notably, no instances of trichomoniasis (pH > 5.5) were observed in either the BT or AT conditions. In the control group, a parallel positive

trajectory was observed. Prior to treatment, none of the participants presented with a normal pH level. Post-treatment, however, a significant 80.77% achieved a normal pH level, underscoring a substantial improvement according to the Wilcoxon matched pair test (p-value < 0.0001). Furthermore, the prevalence of bacterial vaginosis diminished from 96.15% to 15.38% after treatment, as indicated by the Wilcoxon matched pair test (p-value < 0.0001). Similar to the test group, no instances of trichomoniasis were observed in either BT or AT. Upon scrutinizing the test and control groups before treatment, no statistically significant differences in the distribution of pH-associated conditions were discerned (Fisher's Exact test; P-value = 0.34). However, a noteworthy borderline statistical divergence became apparent after treatment, with a P-value of 0.05 in the Fisher's Exact test. The fact that 100% of patients transitioned to a normal pH after the test treatment, while 80.77% achieved the same in the control group, underscores a higher efficacy and success rate in normalizing pH levels with the test treatment. This suggests a notable and statistically significant difference in the effectiveness of the two treatments in addressing bacterial vaginosis and restoring a normal pH environment. Evidently, within the test group, a notable transformation in the distribution of vaginal pH levels was evident post-treatment. This is according to the study of AL-Maliki RS et al. who likewise to our study attributed the changes in pH to anti-microbial properties, antioxidant activity, and anti-fungal properties as seen in the phytochemistry of the compound formulation.[28]Our study also revealed a notable correlation between the treatment intervention and changes in pH levels among individuals with Bacterial Vaginosis (BV). In the test group, the mean pH for BV cases declined significantly from 4.78 ± 1.2 before treatment to 3.89 ± 0.9 after treatment. Similarly, in the control group, BV cases showed a reduction in mean pH levels from 4.89 ± 2.2 before treatment to 3.98 ± 1.09 after treatment. These findings align with existing knowledge linking elevated vaginal pH (above 4.5) to BV onset, attributed to the replacement of normal vaginal lactobacilli by anaerobic bacteria.[29,30] The observed reduction in pH levels post-treatment suggests a potential therapeutic impact on the pH imbalance associated with BV. Elevated vaginal pH has been linked to changes in microbial status during vaginal infections, as reported in previous studies, such as the investigation conducted by Hanna et al. in 1985.[31] The comparative analysis between the test and control groups revealed that both treatments were effective in reducing the severity of vaginal discharge and improving Pap smear, Gram staining, Nugent scores, and KOH preparation results. However, the test drug consistently showed superior outcomes, particularly in the normalization of Pap smear results and the reduction of Nugent scores.. Moreover, it is

noteworthy that all safety parameters, including CBC, LFT, and KFT, remained stable throughout the treatment course, underscoring the safety profile of the intervention.

Conclusion

The findings of this study provide robust evidence that the test drug is highly effective in treating Sayalān al -Raḥim, demonstrating substantial improvements across various clinical parameters. The superior performance of the test drug, especially in achieving normal Pap smear results and favorable bacterial flora composition, underscores its potential as a preferred treatment option. The test drug's antifungal, antioxidant, and antimicrobial properties contributed to its effectiveness. Safety parameters remained stable, underscoring the formulation's safety profile. These findings suggest that the test drug may offer enhanced therapeutic benefits over standard treatments, contributing to better patient outcomes in clinical practice. Further studies with larger sample sizes and long-term follow-ups are recommended to confirm these results and explore the broader implications of these findings in different populations.

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