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# Comparative evaluation of efficacy and safety of A Unani coded drug UNIM-221 and Metformin in cases of Diabetes mellitus type-II: A preliminary study

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**Abstract**
Diabetes mellitus is a major public health problem affecting millions of people worldwide. Available synthetic medicines have serious side effects, therefore, medicines of herbal origin have been widely used in therapeutic management of diabetes mellitus for a long time, and have received renewed attention of scientists globally. The present study envisages to evaluate the comparative efficacy and safety of a Unani coded drug UNIM-221 with an allopathic drug Metformin in diabetes mellitus type II cases. The data presented is a part of multicentric, randomized and open level clinical trials conducted on 32 UNIM-221and 44 cases on Metformin at Regional Research Institute of Unani Medicine, Aligarh, during 2013-2018. The statistical analysis of data presented was done by using one-way analysis of variance (ANOVA) followed by Dennett's' test and, p value of ≤0.05 was considered significant. The results were compared with baseline to different follow-up of two groups of diabetes patients treated with Unani and allopathic drug, namely, UNIM-221 and Metformin. We conclude that UNIM-221 has shown a significant and better relief in various symptoms of diabetes mellitus patients *viz*; polydipsia, polyuria, polyphagia, nocturia, fatigue, loss of weight, burning sensation in palm and soles and giddiness as compared to allopathic drug Metformin. Thus, whereas both the drugs do possess antidiabetc activity and reduce blood glucose level and HbA1c level, respectively, yet the Unani drug UNIM-221 has shown comparatively better rate of efficacy and safety and, therefore, recommended for long time use in diabetes mellitus type II cases without any side effects. Further studies are suggested on a larger group.

**Keywords:** Diabetes mellitus type II, UNIM-221, metformin, temperament (mizaj), glycosylated haemoglobin (HbA1C)

## Introduction
Diabetes mellitus (*Ziabetes shakari*) is a metabolic disorder of multiple diagnoses, specified by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism as a result from defects in insulin secretion, insulin action, or both [1]. In 2000, India (31.7 million) superimposed the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. The prevalence of diabetes is predicted to two times globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India [2]. It is concluded that by 2030 diabetes mellitus may burden up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see important increase in those affected by the disease [2, 3]. In allopathic system, a vast range of oral anti-diabetic drugs are now accessible for the management of diabetes. These classes comprise of those agents that trigger insulin secretion (Sulphonylurea and rapid acting secretagogues), lower hepatic glucose production (biguanides), retard digestion and absorption of intestinal carbohydrate (alpha-glucosidase inhibitors) or enhance insulin action (thiazolidinediones). These drugs regulate the blood sugar level as long as they are consistently administered but produce a number of unwanted adverse effects [4].
In Unani system of medicine many drugs (mufradat) (single drugs) including Gul surkh (*Rosa damascena* Mill.), Gulnaar (*Punica granatum* Linn.), *Roghane gul* (*Rosa damascena*), Roghane Neelufar (*Nymphaea alba* Linn*)*, Aabe Jangali Kaasni (*Cichorium intybus* Linn.), Gile Armani (*Armenian bole*), Sandal Safed (*Santalum album* Linn), Tukhme khurfa (*Portulaca oleracea* Linn*.)*, Tukhme kahu *(Lactuca sativa* Linn.), Rubb Angoor Khaam (*Vitis vinifera* L.), Aabe Khurfa Sabz (*Portulaca oleracea* Linn), Loabe Isapghol

(*Plantago ovata* Forsk), Kishneez Khushk (*Coriandrum sativum* Linn.) [5] and compound Unani drugs (Murakkabat) such as *Sufoof-i-Ziabetus, Kushta Zamarrud, Qurs-i-Kafoor, Qurs-i-Tabasheer, Sufoof-i-Sandal Ziabetus Wala, Qurs-i- Ziabetus, Arq-i- Ziabetus, Ma-us-Sha'eer, Qurs-i-Tabasheer-Kafoori, Qurs-i- Ziabetus Khas, Qurs-i- Ziabetus Sada* had been used for treatment of diabetes mellitus [6] for centuries.

Thus present study is focused on a Unani formulation due to its versatile role in diabetes with no or negligible adverse effects and cost effectiveness, in treatment of diabetes mellitus type II or NIDDM [7, 8]. According to Unani literature Ziabetus Shakari (diabetes mellitus) is characterized by excessive thirst, excessive urination [9, 10, 11], presence of sugar in urine, increased appetite, gradual loss of body weight, and so forth [11, 12]. Decreased sexual functions and gangrene are noted complications [10]. The main causes of Ziabetus Shakari are sue mizaj haar (extreme hot derangement of temperament) and weakness of quwwate maseka (retentive power) of the kidney [9, 13], hararate naria [12], sue mizaj barid (cold derangement of temperament) of the kidney or whole body, zoafe gurda (weakness of the kidney), and dilatation of ducts and vessels of the kidney [14].

## Materials and Methods

### Study design

Multicentric, randomized and open level clinical trial. This study is a part of multicentric clinical trial of test drug UNIM-221 conducted at Regional Research Institute of Unani Medicine, Aligarh during 2013-2018. Both the drugs UNIM-221 and allopathic Metformin were procured from Central Council for Research in Unani Medicine, New Delhi. In trial group, total cases completed were 65, out of which 32 cases gave good response and 28 moderate response. In control group, out of 72 cases, 44 gave good response and 28 showed moderate response. The patients attended the out patients departments (OPD) of Institute were of either sex, age (18-65 yrs). After screening, following inclusion and exclusion criteria, patients were randomized into two groups according to a block randomized schedule. This project was approved by institutional ethics committee of Regional Research Institute of Unani medicine (RRIUM), Aligarh, on 26-03-2013 (Ref: 5-11/2011-12/RRI-ALG/Tech/35) and is also registered in Clinical Trials Registry-India (CTRI) (Ref: CTRI/2013/10/004092).

### Subject selection

A diabetes mellitus type-II patient having all the inclusion and exclusion criteria was invited to participate in the study.

### Inclusion Criteria

Patients of either sex in the age group of 18-65 years. Patients having fasting glucose level between 126 to 150 mg/dl and post prandial glucose level between 200 to 250 mg/dl after two hours after meals and glycosylated haemoglobin (HbA1c) ≥ 6.5%. Patients having any of the following signs and symptoms of diabetes mellitus *viz*; *Utash mufrit* (polydipsia), *Kasrat-al-Bawl* (polyuria), *Kasrat-al-Ishtiha* (polyphagia), *Bawl Layli* (nocturia), *I'ya* (fatigue), *Naqs al-Wazn* (loss of weight), Burning sensation in palm and soles, Sadr (giddiness) and *Naqs al-Shahwa* (loss of libido). All the symptoms and signs had been graded on the ten point visual analog scale (VAS). Severity in ten point visual analog scale for all, except loss of weight which was recorded in numbers.

### Exclusion criteria

Patients having insulin therapy, diabetes mellitus type-I, associated with complications of ketoacidosis, Ischemic heart disease/hypertension/hyperlipidemia, malignancy/epilepsy or any infective disorder, drug addicts/alcoholics were excluded. Patients taking systemic corticosteroids/ disease modifying agents. Patients having fasting glucose > 150 mg/dl and post prandial glucose level > 250 mg/dl and in case anaemia, patients having Hb<8 gm/dl in males and Hb<6 gm/dl in females, Obese patients with BMI>30. Patients having liver disorders SGPT>105 IU/L, Impaired renal function tests, pregnant and lactating women were excluded. Patients taken any other treatment including use of alternative medicine were also excluded.

### Drug, dose and mode of administration

One group of patients was orally administered Unani coded drug UNIM-221 in the form of granules of 10 gm whereas, the other group, was given one tablet of metformin (500mg) to diabetic patients orally with water twice a day before 30 minutes of meals for a period of 12 weeks. The signs and symptoms were recorded on 1st-day, 2-week, 4-week, 6-week, 8-week, 10-week and 12th week whereas biochemical and hematological investigations were conducted on day-first and at the end of the study i.e. after 12 weeks.

### Assessment of *mizaj* (temperament)

In both the groups, assessment of *mizāj* (temperament) was done at baseline (Tabe-1).

### Criteria for efficacy of evaluation

1. Improvement in the following signs and symptoms in diabetes mellitus type II patients.
   - *Utash mufrit* (polydipsia).
   - *Kasrat-al-Bawl* (polyuria).
   - *Kasrat-al-Ishtiha* (polyphagia).
   - *Bawl Layli* (nocturia).
   - *I'ya* (fatigue).
   - *Naqs al-Wazn* (loss of weight).
   - Burning sensation in palm and soles.
   - Sadr (giddiness).
   - *Naqs al-Shahwa* (loss of libido).
2. Reduction in fasting and post-prandial (PP) blood sugar level.
3. Decrease in HbA1c level by ≥ 1.0% as compared to baseline.

### Biochemical studies

Biochemical investigations were done following well established laboratory tests as under:

Glucose by Trinder's method [15], glycosylated haemoglobin (HbA1c) by ADACPR 2010 [16], serum glutamate pyruvate transaminase (SGPT, E.C. 2.6.1.2) and serum glutamate oxaloacetate transaminase (SGOT, E.C. 2.6.1.1.) were done by the method described by International Federation of Clinical Chemistry (IFCC) [17], serum alkaline phosphatase enzyme (S-ALP, EC. 3.1.3.1) by the method of Wilkinson *et al.* (1969) [18], blood urea nitrogen (BUN) by the method of Tiffany *et al.* (1972) [19], serum creatinine by Bowers (1980) method [20], serum total bilirubin by modified method of

Pearlman & Lee (1974) [21], uric acid by modified Trinder peroxidase Method [22], cholesterol by modified Roeschlau's method [23], triglycerides by Fossati *et al*, (1969) [24], total protein by Tietz (1986) [25], and albumin by Doumas *et al.* (1972) [26].

**Haematological studies**

Haematological parameters were done according to the method described by Mukherjee (1990) [27]. These included haemoglobin (Hb), erythrocyte sedimentation rate (ESR), total leucocytes counts (TLC), red blood corpuscles (RBC), platelet counts and differential leucocytes counts (DLC): polymorphs, lymphocytes and eosinophil counts.

**Collection of blood serum**

Blood samples were collected by puncturing the vein at each investigation. 1.0 ml of blood with ethylene diamine tetra acetic acid (EDTA) was used for various haematological parameters and another 2.0-2.5 ml of blood sample was allowed to clot and serum was separated by centrifugation, which was used for different biochemical investigations.

**Statistical analysis**

Data were analyzed statistically by using one-way analysis of variance (ANOVA) followed by Dennett's' test. The values were considered significant when the P- value was found less than 0.05.

**Results and Discussion**

**Demographic Study**

In trial group, out of 32 patients of diabetes mellitus type-II (*Ziabetes Sukkari Qism-e-Sani*), 21(51.90%) were male and 11 (48.91%) female, whereas in control group, 27(61.36%) were male and 17 (30.64%) female, which shows that males have higher incidence as compared to female. Similar conclusion had been reported by others workers [28, 29]. It is due to larger amount of visceral fat in men than in women. In both trial as well as control group of patients with age group 41-50 years were 11 (34.38%) and 22 (50.00%) respectively have higher incidence followed by age group 51-60 years 12 (37.50%) and 12 (27.27%) respectively (table-1). Similar statement had been given by other workers [30]. Risk factors comprise of family history, body mass index (BMI), smoking, tobacco chewing and alcohol intake. In both trial and control groups, 10 (31.25%) and 13 (29.55%) of patients respectively had family history of diabetes. In both trial and control group, 25 (78.13%) and 30 (68.18%) (table-1) respectively had BMI greater than or equal. Similar interpretation had been reported by other authors [31].

In both trial and control group, 02 (6.25%) and 04 (9.10%) of patients respectively had smoking habits, whereas 05 (15.63%) and 06 (13.64%) (table-1) of patients respectively had tobacco chewing habit. Some authors had reported that there was an association between cigarette smoking, hyperglycemia and development of diabetes type 2 [32]. In dietary habit of both trial and control group, non-vegetarians 22 (68.75%) and 32 (72.73%) had more incidence than vegetarians 10 (31.25%) and 12 (27.27%) (Table-1) respectively. Diet high in red and processed meats, refined grains, and other characteristics of the western pattern was associated with an elevated risk of type 2 diabetes mellitus in women.

Red and processed meats were also independently associated with an increased risk [33]. Vegetarian diets (vegan, lacto-ovo, and pesco- and semi-vegetarian) were associated with substantially lower risk of type 2 diabetes and lower BMI than non-vegetarian diets [34]. In assessment of temperament (mizaj) of both trial and control group, the incidence was more or equal in Damwi (Sanguine) 12 (37.50%) and 20 (45.46%) as compared to Safrawi (Bilious) 12 (37.50%) and 19 (43.18%) followed by Balghami (Phlegmatic) 08 (25.00%) and 05 (11.36) respectively (table-1). Similar type of interpretation had been made by other workers [35].

**Biochemical Studies**

**Safety assessment**

**Effect on liver and kidney function tests**

The biochemical investigations revealed that there were no significant changes in liver function tests as well as kidney function tests. Therefore, can be inferred that the both the test drug as well as allopathic drug did not induce any negative or unfavorable response. The safety of the drug is therefore conformed (Table-6).

**Assessment of efficacy**

**Clinical studies**

When one group of Unani coded drug UNIM-221 in the form of granules of 10 gm whereas other group, one tablet of metformin (500mg) were given to patients orally with water twice a day before 30 minutes meals for a period of 12 weeks respectively, in both the groups, the effected changes in various diabetic signs and symptoms were recorded and follows as under:

**Subjective parameters**

**Utash Mufrit (polydipsia)**

A significant reduction in score 69.82% ($P<0.0001$)) on $10^{th}$-week and 85.06% ($P<0.0001$) $12^{th}$-week and 31.00% ($P<0.05$) on $4^{th}$ week, 47.14% ($P<0.0001$) on $6^{th}$ week, 58.07% ($P<0.0001$) on $8^{th}$ week, 64.84% ($P<0.0001$) on $10^{th}$ week and 72.40% ($P<0.0001$) on $12^{th}$ week respectively had been observed, and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other authors [35, 36, 37].

**Kasrat al-Bowl (Polyurea)**

A significant reduction in score 42.39% ($P<0.05$)) on $6^{th}$-week, 49.65% ($P<0.05$) $8^{th}$-week, 64.87% (<0.0001) $10^{th}$-week and 81.97% ($P<0.0001$) and $12^{th}$-week and 29.32% ($P<0.05$) on $4^{th}$ week, 52.05% ($P<0.0001$) $6^{th}$ week, 49.10% ($P<0.0001$) $8^{th}$ week, 74.10% ($P<0.0001$) on $10^{th}$ week and 92.27% ($P<0.0001$) on $12^{th}$ week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other workers [35, 36, 37].

**Kasrat al-Ishtiha (polyphagia)**

A significant reduction in score 59.85% (<0.0001) on $10^{th}$-week and 75.45% ($P<0.0001$) on $12^{th}$-week and 37.17% ($P<0.05$) on $4^{th}$ week, 39.23% ($P<0.05$) on $6^{th}$ week, 43.95% ($P<0.01$) $8^{th}$ week, 56.34% ($P<0.0001$) on $10^{th}$ week and 64.90% ($P<0.0001$) on $12^{th}$ week respectively had been observed, and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4

and Fig-1). Similar observation had been reported by other workers [35, 36, 37].

**Bowl layli (Nocturia)**

A significant decrease in score 33.43% (<0.05) on 8th-week and 59.14% ($P$<0.0001) on 10th-week, 68.86 ($P$<0.0001) on 12th week and 37.10% ($P$<0.001) on 6th week, 30.22% ($P$<0.05) on 8th week, 51.10% ($P$<0.0001) 10th week, 59.19% ($P$<0.0001) on 12th week respectively had been observed, and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other authors [35, 36, 37].

**I'ya (fatigue)**

A significant decrease in score 35.10% (<0.05) on 6th-week and 42.86% ($P$<0.01) on 8th-week, 46.68% ($P$<0.0001) on 10th week and 68.41% ($P$<0.001) on 12th week and 34.57% ($P$<0.01) on 6th week, 41.98% ($P$<0.0001) 8th week, 54.57% ($P$<0.0001) on 10th week and 74.07% ($P$<0.0001) on 12th week respectively had been observed, and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other workers [35, 36, 37].

**Effect on Naqs aI Wazn (loss of weight)**

A significant decrease in score 59.04% (<0.05) on 6th-week, 86.35% ($P$<0.0001) on 8th-week, 95.56% ($P$<0.0001) on 10th week, 72.70% ($P$<0.05) on 12th week had been observed whereas a non significant reduction in score had been observed in metformin treated patients in different follow-up, and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other authors [35, 36, 37].

**Effect on burning sensation in palms and soles**

A significant decrease in score 46.67% (<0.05) on 4th-week and 43.14% ($P$<0.05) on 8th-week, 67.84% ($P$<0.0001) on 10th week, 76.86% ($P$<0.0001) on 12th week and 61.10% ($P$<0.01) on 6th week, 46.61% ($P$<0.05) on 10th week, 72.40% ($P$<0.0001) 12th week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other workers [35, 36, 37].

**Effect on Sdar (giddiness)**

A significant decrease in score 56.73% ($P$<0.05) on 6th-week, 68.00% ($P$<0.0001) on 10th-week, 95.64% ($P$<0.0001) on 12th week and 54.89% ($P$<0.05) on 6th week, 52.34% ($P$<0.05) on 10th week, 87.66% ($P$<0.0001) 12th week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3, 4 and Fig-1). Similar observation had been reported by other workers [35, 36, 37].

**Objective parameters**

**Effect on blood glucose fasting**

A significant reduction in the level of blood glucose fasting 12.06% ($P$<0.05) on 6th-week, 10.76% ($P$<0.05) on 2th-week, 10.34% ($P$<0.05) on 8th-week, 14.01% ($P$<0.0001) on 10th-week, 16.15% ($P$<0.0001) on 12th-week and 10.76% ($P$<0.05) on 2th-week, 13.45% ($P$<0.0001) on 6th-week, 16.96% ($P$<0.0001) on 8th-week, 16.98% ($P$<0.0001) on 10th-week, 20.00% ($P$<0.0001) on 12th-week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-5 and Fig-2). Similar observation had been reported earlier by other authors [38, 39, 40].

**Effect on blood glucose post-prandial**

A significant reduction in the level of blood glucose post-prandial 14.00% ($P$<0.001) on 10th-week, 7.72% ($P$<0.05) on 12th-week and 7.33% ($P$<0.05) on 2th-week, 17.06% ($P$<0.001) on 4th-week, 14.48% ($P$<0.001) on 6th-week, 14.83% ($P$<0.001) on 8th-week, 15.19% ($P$<0.001) on 10th-week, 15.33% ($P$<0.001) on 12th-week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-5 and Fig-3). Similar observation had been reported by other workers [38, 39, 40].

**Effect on glycosylated haemoglobin (HbA1c)**

When one group of Unani coded drug UNIM-221 in the form of granules of 10 gm whereas other group, one tablet of metformin (500mg) were given to patients orally with water twice a day before 30 minutes meals for a period of 12 weeks respectively, in both the groups, a significant reduction in the level of glycosylated haemoglobin 8.42% ($P$<0.001) and 11.42% ($P$<0.001) respectively had been observed and these were compared with the values of baseline (1st-day) and post-treatment (84th day) (Table-5). Similar interpretation had been reported by earlier authors [35, 37].

**Effect on lipid and protein profile**

No significant changes in lipid (cholesterol and triglycerides) and protein profile (protein, albumin, globulin and A/G ratio) respectively had been observed (Table-7).

**Effect on Haemogram**

No significant changes in the level of haemoglobin, red blood corpuscles (RBC), total leucocytes count (TLC), platelets count, polymorphs, lymphocyte, eosinophils and erythrocyte sedimentation rate (ESR) respectively had been observed (Table-8).

**Table 1:** Comparative demographic data of trial (UNIM-221) and control (metformin) groups in diabetes mellitus type II patients.

| Variable ↓ Group → | | Trial Group: UNIM-221 No. of patients & percentage n=32 | Control Group: Metformin no. of patients & percentage n=44 |
|---|---|---|---|
| 1. sex | Female | 11(48.91%) | 17(30.64%) |
| | Male | 21(51.90%) | 27(61.36%) |
| 2. Age in Years i. 30-40 | | 05 (15.63%) | 04 (9.09%) |
| ii. 41-50 | | 11 (34.38%) | 22 (50.00%) |
| iii.51-60 | | 12 (37.5%) | 12 (27.27%) |
| iv. 61-65 | | 04 (12.5%) | 06 (13.64%) |

| | | |
|---|---|---|
| 3.Duration of Disease: i. 1.0 month to 1.0 Year | 28 (87.50%) | 39 (88.64) |
| ii. 1.1 Year to 3.0-years | 03 (9.38%) | 04 (9.10%) |
| iii >3.0 Years | 01 (3.13%) | 01 (2.27%) |
| 4.Risk Factors i. Family History | 10 (31.25%) | 13 (29.55%) |
| ii. BMI ≥ 25Kg/$m^2$ | 25 (78.13%) | 30 (68.18%) |
| iii Smoking | 02 (6.25%) | 04 (9.10%) |
| iv. Tobacco | 05 (15.63%) | 06 (13.64%) |
| v. Alcohol | 01 (3.13%) | Nil |
| 5.Dietary habits i. Vegetarian | 10 (31.25%) | 12 (27.27%) |
| ii. Non-Vegetarian | 22 (68.75%) | 32 (72.73%) |
| 6. Assessment of mizaj (Temperament): i. Balghmi Phlegmatic) | 08(25.00%) | 05(11.36%) |
| ii. Damvi (Sanguine) | 12(37.50%) | 20(45.46%) |
| iii. Safrawi (Bilious) | 12(37.50%) | 19(43.18%) |
| iv. Saudawi (Melancholic) | Nil | Nil |

**Table 2:** Effect of Unani coded drug UNIM-221(trial group) in improving symptoms in diabetes mellitus type II patients.

| Treatment → Symptom ↓ | Baseline (0-Day) | 1st F-up (2-week) | 2nd F-up (4-week) | 3rd F-up (6-week) | 4rth F-up (8-week) | 5th F-up (10-week) | 6th F-up (12-week) |
|---|---|---|---|---|---|---|---|
| 1. *Utash Mufrit* (polydipsia) n=21 | 3.48 ±0.76 | 3.38 ±0.58$^{\bullet}$ | 2.86 ±0.57$^{\bullet}$ | 2.33 ±0.64$^{\bullet}$ | 1.86 ±0.54$^{\bullet}$ | 1.05 ±0.42$^{**}$ | 0.52 ±0.24$^{***}$ |
| 2. *Kasrat al-Bowl* (polyurea) n=26 | 4.27 ±0.66 | 4.35 ±0.49$^{\bullet}$ | 3.19 ±0.55$^{\bullet}$ | 2.46 ±0.54$^{*}$ | 2.15 ±0.53$^{*}$ | 1.50 ±0.44$^{***}$ | 0.77 ±0.33$^{***}$ |
| 3. *Kasrat al-Ishtiha* (polyphagia) n=23 | 3.91 ±0.65 | 4.13 ±0.59$^{\bullet}$ | 2.70 ±0.63$^{\bullet}$ | 2.39 ±0.61$^{\bullet}$ | 2.35 ±0.57$^{\bullet}$ | 1.57 ±0.40$^{***}$ | 0.96 ±0.27$^{***}$ |
| 4. *Bowl Layli* (nocturia) n=30 | 3.50 ±0.50 | 3.33 ±0.42$^{\bullet}$ | 2.80 ±0.43$^{\bullet}$ | 2.37 ±0.42$^{\bullet}$ | 2.33 ±0.30$^{*}$ | 1.43 ±0.26$^{***}$ | 1.37 ±0.26$^{***}$ |
| 5. *I'ya (*fatigue) n=31 | 4.97 ±0.59 | 4.52 ±0.56$^{\bullet}$ | 3.58 ±0.55$^{\bullet}$ | 3.23 ±0.49$^{*}$ | 2.84 ±0.54$^{**}$ | 2.65 ±0.47$^{***}$ | 1.57 ±0.35$^{***}$ |
| 6. *Naqs al Wazn* (loss of weight) n=15 | 2.93 ±0.69 | 1.93 ±0.78$^{\bullet}$ | 1.93 ±0.65$^{\bullet}$ | 1.20 ±0.48$^{*}$ | 0.40 ±0.29$^{***}$ | 0.13 ±0.13$^{***}$ | 0.80 ±0.67$^{*}$ |
| 7. Burning sensationin palms and soles n=22 | 2.55 ±0.42 | 1.27 ±0.34$^{\bullet}$ | 1.36 ±0.35$^{*}$ | 1.64 ±0.36$^{\bullet}$ | 1.45 ±0.26$^{*}$ | 0.82 ±0.20$^{***}$ | 0.59 ±0.21$^{***}$ |
| 8. *Sdar* (giddiness) n=16 | 2.75 ±0.50 | 2.12 ±0.45$^{\bullet}$ | 2.12 ±0.40$^{\bullet}$ | 1.19 ±0.38$^{*}$ | 0.81 ±0.33$^{***}$ | 0.88 ±0.31$^{***}$ | 0.12 ±0.12$^{***}$ |

[$^{*}P$<0.05, $^{**}P$<0.01 are significant, $^{***}P$<0.001 is highly significant and $^{\bullet}$P is not significant]

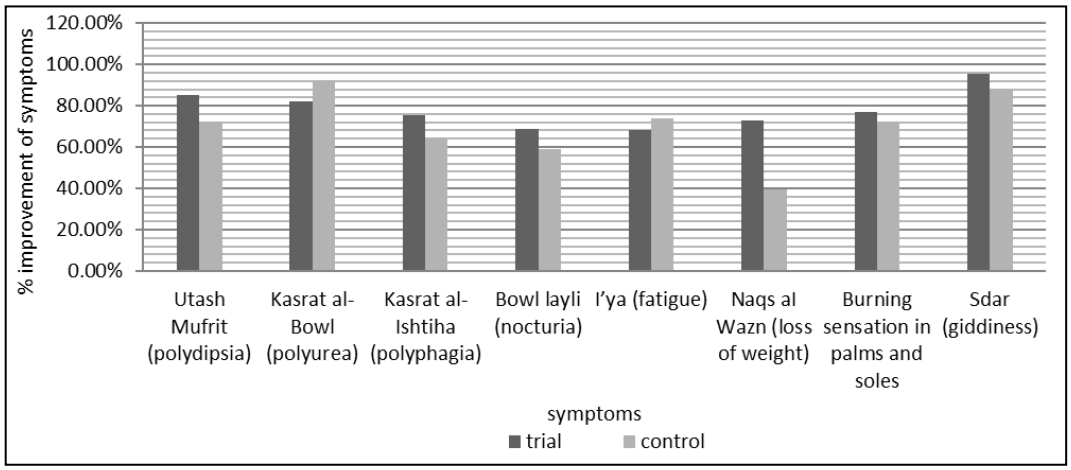


**Fig 1:** Comparative data showing percentage improvement of signs and symptoms in trial and control groups in diabetes mellitus type-II patients

**Table 3:** Effect of allopathic drug Metformin in improving symptoms in diabetes mellitus type II patients.

| Treatment → Symptom ↓ | Baseline (1st -Day) | 1st F-up (2-week) | 2nd F-up (4-week) | 3rd F-up (6-week) | 4rth F-up (8-week) | 5th F-up (10-week) | 6th F-up (12-week) |
|---|---|---|---|---|---|---|---|
| 1. *Utash Mufrit* (polydipsia) n=32 | 3.84 ±0.46 | 3.23 ±0.39$^{\bullet}$ | 2.65 ±0.41$^{*}$ | 2.03 ±0.37$^{***}$ | 1.61 ±0.30$^{***}$ | 1.35 ±0.30$^{***}$ | 1.06 ±0.27$^{***}$ |
| 2. *Kasrat al-Bowl* (polyurea) n=35 | 4.40 ±0.42 | 3.37 ±0.43$^{\bullet}$ | 3.11 ±0.34$^{*}$ | 2.11 ±0.36$^{***}$ | 2.24 ±0.38$^{***}$ | 1.14 ±0.27$^{***}$ | 0.34 ±0.15$^{***}$ |
| 3. *Kasrat al-Ishtiha* (polyphagia) n=31 | 3.39 ±0.40 | 2.55 ±0.45$^{\bullet}$ | 2.13 ±0.44$^{*}$ | 2.06 ±0.42$^{*}$ | 1.90 ±0.40$^{**}$ | 1.48 ±0.41$^{***}$ | 1.19 ±0.32$^{***}$ |
| 4. *Bowl Layli* (nocturia) n=42 | 3.21 ±0.31 | 2.62 ±0.30$^{\bullet}$ | 2.43 ±0.31$^{\bullet}$ | 2.02 ±0.26$^{**}$ | 2.24 ±0.29$^{*}$ | 1.57 ±0.26$^{***}$ | 1.31 ±0.23$^{***}$ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 5. *I'ya* (fatigue) n=43 | 4.05 ±0.39 | 3.37 ±0.40▪ | 3.09 ±0.38▪ | 2.65 ±0.35** | 2.37 ±0.34*** | 1.84 ±0.32*** | 1.05 ±0.22*** |
| 6. *Naqs al Wazn* (loss of weight) n=19 | 1.84 ±0.49 | 1.05 ±0.41▪ | 1.26 ±0.43▪ | 1.16 ±0.41▪ | 1.16 ±0.39▪ | 0.95 ±0.37▪ | 1.11 ±0.29▪ |
| 7. Burning sensation in palms and soles n=28 | 2.21 ±0.38 | 2.18 ±0.39▪ | 1.50 ±0.26▪ | 0.86 ±0.27** | 1.46 ±0.31▪ | 1.18 ±0.30* | 0.61 ±0.17*** |
| 8. *Sdar* (giddiness) n=17 | 2.35 ±0.51 | 1.71 ±0.38▪ | 1.06 ±0.36▪ | 1.06 ±0.34* | 1.41 ±0.30▪ | 1.12 ±0.32* | 0.29 ±0.17*** |

[*$P$<0.05, **$P$<0.01 are significant, ***$P$<0.001 is highly significant and ▪P is not significant]

**Table 4:** Comparative data of Unani and modern drugs: showing percentage improvement of symptoms of trial and control groups in diabetes mellitus type-II patients.

| S. No. | Symptoms | UNIM-221 | Metformin |
|---|---|---|---|
| | | (Percentage improvement of symptom at 12th-week from baseline) | |
| 1 | *Utash Mufrit* (polydipsia) | 85.06% | 72.40% |
| 2 | *Kasrat al-Bowl* (polyurea) | 81.97% | 92.27% |
| 3 | *Kasrat al-Ishtiha* (polyphagia) | 75.45% | 64.90% |
| 4 | *Bowl layli* (nocturia) | 68.86% | 59.19% |
| 5 | *I'ya* (fatigue) | 68.41% | 74.07% |
| 6 | *Naqs aI Wazn* (loss of weight) | 72.70% | 39.68% (reduction but not significant) |
| 7 | Burning sensation in palms and soles | 76.86% | 72.40% |
| 8 | *Sdar* (giddiness) | 95.64% | 87.66% |

**Table 5:** Comparative effect of Unani coded drug UNIM-221 and allopathic drug Metformin in the level of fasting blood glucose in diabetes mellitus type II.

| Parameter Group ▼ ▼ | | Baseline (1st -Day) | 1st F-up (2-week) | 2nd F-up (4-week) | 3rd F-up (6-week) | 4rth F-up (8-week) | 5th F-up (10-week) | 6th F-up (12-week) |
|---|---|---|---|---|---|---|---|---|
| Blood glucose fasting (mg %) | UNIM-221 | 153.80 ±5.90 | 147.82 ±6.89▪ | 144.13 ±8.57▪ | 135.25 ±5.94* | 137.90 ±6.41* | 132.26 ±4.42*** | 128.96 ±4.67*** |
| | Metformin | 147.68 ±3.80 | 131.79 ±7.15* | 152.61 ±30.30▪ | 127.82 ±5.26*** | 122.63 ±3.88*** | 122.60 ±3.85*** | 118.31 ±2.98*** |
| Blood glucose post-prandial (mg %) | UNIM-221 | 234.88 ±6.17 | 231.96 ±10.33▪ | 228.49 ±11.07▪ | 219.67 ±8.93▪ | 226.52 ±10.35▪ | 202.14 ±7.40*** | 216.75 ±8.15* |
| | Metformin | 235.43 ±6.22 | 218.18 ±7.38* | 195.26 ±8.33*** | 201.35 ±7.88*** | 200.51 ±7.69*** | 199.68 ±8.67*** | 199.35 ±7.66*** |
| Glycosylated haemoglobin (HbA1c) (%) | UNIM-221 | 7.13 ±0.20 | | | | | | 6.53 ±0.12*** |
| | Metformin | 6.74 ±0.14 | | | | | | 5.97 ±1.21*** |

[*$P$<0.05, **$P$<0.01 are significant, ***$P$<0.001 is highly significant and ▪P is not significant]

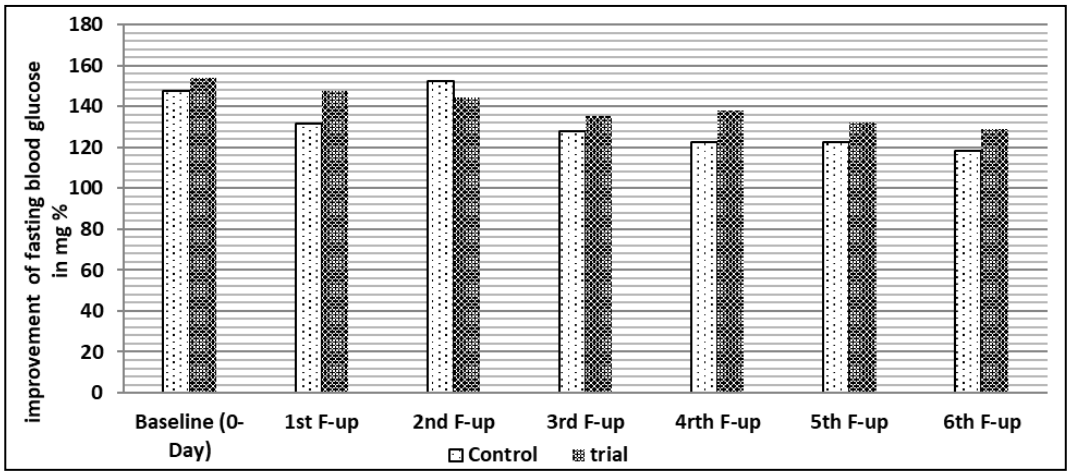


**Fig 2:** Comparative effect of allopathic drug metformin (control group) and Unani coded drug UNIM-221 in the level of fasting blood glucose in diabetes mellitus type II patients.

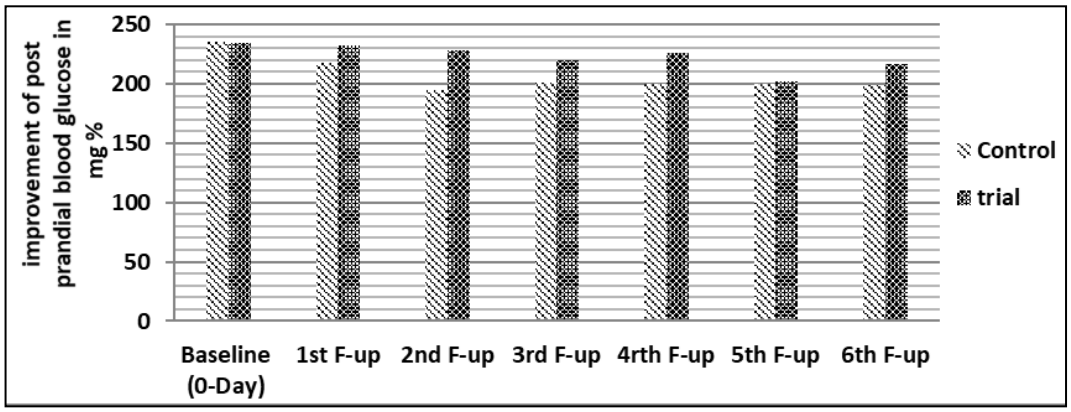


**Fig 3:** Comparative effect of allopathic drug metformin (control group) and Unani coded drug UNIM-221 (trial group) in the level of post prandial blood glucose of diabetes mellitus type II patients.

**Table 6:** Comparative effect of Unani coded drug UNIM-221 and allopathic drug Metformin in the levels of SGPT, SGOT and serum alkaline phosphatase, blood urea nitrogen (BUN) and serum creatinine in diabetes mellitus type II patients.

| Group ↓ Parameter → | | SGPT (IU/L) | SGOT (IU/L) | Alkaline Phosphatase (IU/L) | Bilirubin (mg %) | Blood Urea Nitrogen (BUN) (mg %) | Creatinine (mg %) | Uric Acid (mg %) |
|---|---|---|---|---|---|---|---|---|
| UNIM-221 | Baseline (1st -Day) | 29.31±5.32 | 25.98±3.89 | 83.30±4.35 | 0.74±0.04 | 27.39±2.14 | 1.06±0.05 | 4.71±0.20 |
| | End follow-up (12th-week) | 27.45±2.15* | 23.88±1.74* | 74.33±4.06* | 0.76±0.04* | 23.70±1.92* | 1.01±0.27* | 4.85±1.92* |
| Metformin | Baseline (1st -Day) | 29.52±2.24 | 27.10±1.80 | 80.50±4.00 | 0.79±0.03 | 22.96±1.74 | 0.99±0.03 | 4.61±0.20 |
| | End follow-up (12th-week) | 26.35±2.30* | 26.02± 1.45* | 85.96±5.83* | 0.77±0.03* | 21.76±1.83* | 1.00±0.04* | 4.65±0.19* |

[*P is not significant]

**Table 7:** Comparative effect of Unani coded drug UNIM-221 and allopathic drug Metformin in the level of cholesterol, triglycerides, protein, albumin, globulin and A/G ratio in diabetes mellitus type II patients.

| Parameter → Group ↓ | | Cholesterol (mg %) | Triglycerides (mg %) | Protein (gm %) | Albumin (gm %) | Globulin (gm %) | A/G |
|---|---|---|---|---|---|---|---|
| UNIM-221 | Baseline(1st -day) | 163.69±6.10 | 140.47± 10.25 | 7.03±0.09 | 3.74±0.08 | 3.27±0.09 | **1.18±0.05** |
| | End follow-up (12th-week) | 174.69±6.10* | 139.99±11.91* | 7.14±0.11* | 3.84±0.11* | 3.30±0.11* | **1.21±0.07*** |
| Metformin | Baseline (1st -day) | 174.76±5.66 | 133.61±7.72 | 7.15±0.09 | 3.78±0.06 | 3.38±0.09 | **1.16±0.05** |
| | End follow-up (12th-week) | 167.54±5.60* | 116.80±5.69* | 7.18±0.08* | 3.82±0.06* | 3.30±0.11* | **1.24±0.07*** |

[*P is not significant]

**Table 8:** Comparative effect of Unani coded drug UNIM-221 and allopathic drug metformin in the level of haemoglobin (Hb), red blood counts R.B.C, total leucocyte counts (TLC), erythrocyte sedimentation rate (ESR), platelets counts, polymorphs, lymphocytes and eosinophils count in diabetes mellitus type II patients.

| Parameter → Group ↓ | | Haemoglobin (gm %) | R.B.C. ($10^6$ /$mm^3$) | T.L.C. ($10^3$/$mm^3$) | E.S.R. (mm /hr) | Platelet Counts (Lac/ $mm^3$) | Differential leucocyte counts (DLC) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Polymorphs (%) | Lymphocytes (%) | Eosinophils (%) |
| UNIM-221 | Baseline (1st -day) | 13.49±0.20 | 4.69±0.08 | 8.38±0.41 | 31.00±2.10 | 2.01±0.13 | 68.00±1.16 | 28.00±1.15 | 4.00±0.37 |
| | End follow-up (12th-week) | 13.45±0.23* | 4.65±0.10* | 8.30±0.49* | 34.00±2.29* | 1.99±0.12* | 69.00±1.24* | 26.00±1.23* | 5.00±0.42* |
| Metformin | Baseline (1st -day) | 12.86±0.23 | 4.43±0.06 | 8.31±0.37 | 38.00±1.97 | 2.19±0.10 | 67.00±1.16 | 28.00±1.14 | 5.00±0.30 |
| | End follow-up (12th-week) | 12.56±0.20* | 4.34±0.05* | 8.2±0.32* | 35.00±1.93* | 2.14±0.10* | 69.00±1.13* | 26.00±1.15* | 5.00±0.35* |

[*P is not significant]

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**Conclusion**
The present study conclusively establishes the efficacy and safety of Unani drug UNIM-221 as compared to allopathic drug metformin and hold promise to a great extent, reducing the sufferings of diabetes mellitus patient's as shown in table-4 fig-1-3.Therefore, the test drug UNIM-221 is recommended for further investigations on a larger group of patients in order to develop a herbal drug of choice to combat diabetes-mellitus which still eludes satisfactory cure in modern medicine.

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