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S Afza
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

P Khan
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

S Rehman
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

S Ayub
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

R Singh
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

RS Verma
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

Jamal Akhtar
Central Council for Research in Unani Medicine, Jawaharlal Nehru Anusandhan Bhavan, 61-65, Institutional Area, Opp. D-Block, Janakpuri, New, India

Asim Ali Khan
Central Council for Research in Unani Medicine, Jawaharlal Nehru Anusandhan Bhavan, 61-65, Institutional Area, Opp. D-Block, Janakpuri, New, India

Corresponding Author:
S Afza
Regional Research Institute of Unani Medicine (CCRUM), Aligarh, Uttar Pradesh, India

Comparative study of efficacy and safety of Unani coded drug UNIM-904 with allopathic drug amlodipine in the treatment of essential hypertension

S Afza, P Khan, S Rehman, S Ayub, R Singh, RS Verma, Jamal Akhtar and Asim Ali Khan

Abstract
Hypertension (known as *Zaghtuddam Qawi Lazmi* in Unani literature) is a major public health issue affecting millions of people worldwide and is also the most prevalent cardiovascular disease risk factor. Available synthetic medicines have serious side effects, therefore, medicines of herbal origin have been extensively used in therapeutic management of hypertension for a long time. The present study aims to evaluate the comparative efficacy and safety of Unani drug UNIM-904 with an allopathic drug amlodipine in essential hypertension cases. The data presented in this work is a part of a multicentric, randomized and open level clinical trial conducted on 41 UNIM-904 and 61 amlodipine cases at Regional Research Institute of Unani Medicine, Aligarh, during 2014-2018. 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 study indicates that when results were compared with baseline to different follow-ups of two groups treated with Unani and allopathic drug, namely, UNIM-904 and amlodipine, the former has shown a significant and much better relief in various symptoms of essential hypertension patients *viz* vertigo, palpitation and laziness as compared to allopathic drug amlodipine. Thus, it is concluded that both the drugs do possess anti hypertensive activity and reduce systolic, diastolic blood pressure and pulse rate, respectively, yet the Unani coded drug has shown comparatively better rate of efficacy, safety and without side effect and, therefore, recommended for use in essential hypertension cases. Further studies are suggested on a larger group of essential hypertensive patients in order to develop safe, effective, viable and cheap herbal drug to combat hypertension evading satisfactory cure in modern medicine.

Keywords: Vertigo, palpitation, essential hypertension **(***Zaghtuddam Qawi Lazmi*), Temperament (MIZAJ)

Introduction
The global burden of hypertension in 2010 was approximately 1.4 billion people and likely to exceed the projected 1.6 billion by 2025 [1, 2]. Cardiovascular diseases (CVD), caused an estimated 25% of India's non-communicable diseases (NCD) burden in 2016. Hypertension is a major threat for CVD, specifically ischemic heart disease and stroke [3, 4]. While the prevalence of hypertension reducing in many high-income countries from 1975 to 2015, it rose generally in most low-income and middle-income countries, and mainly in South Asia [5]. In a recent nationally representative study among 1.3 million adults in India, it is found that 25% of adults had raised blood pressure (BP), with even young adults aged 18–25 years having a substantial prevalence, at 12% [6]. In India there is 24-30% of prevalence of hypertension in urban areas and 12-14% in rural areas [7]. Many variable risk factors for hypertension have been discovered, including being overweight or obese [8, 9], not attending in physical activity [10, 15] and taking a poor diet [11], large amount of alcohol intake [15], use of nonnarcotic analgesics [12, 13], insulin resistance, high salt intake [17] and low folic acid intake [14, 15] have been detected as self dependent original and changeable risk factors for developing hypertension among women. The available treatment of hypertension in modern medicine includes many classes of antihypertensive drugs such as diuretics, beta blockers, calcium channel blockers, ACE inhibitors, vasodilators *etc*. These drugs are capable in controlling the blood pressure of a hypertensive individual but associated with serious side effects such as hyperglycemia, depression, cramps, vomiting, drowsiness, fatigue, dryness of mouth, impotence, dizziness, diarrhea, loss of the taste, leucopenia, and constipation *etc* [16]. In Unani system of medicine, a number of single as well as compound drugs have been used in the therapeutic management of hypertension for centuries such as:

Dawa-us-shifa, Habb-e-Mudirr, Sharbat-e-Buzoori Motadil, Asrol (*Rauwolfia serpentine* L.), Lahsan (*Alium sativum* Linn.), Parshi-aoshan (*Adiantum capillus* Linn.), Tukhm-e-Kharpaza (*Cucumis melo* Linn.) *etc*. have proven their efficacy in controlling blood pressure [17, 18, 19, 20]. This has led to an increased global demand for the Unani drugs over the years because the allopathic drugs have known adverse side effects. Keeping these in view the present work deals with comparative study on efficacy and safety of Unani coded drug *UNIM-904* with allopathic drug amlodipine in the treatment of essential hypertension and results are presented.

Methodology

Study design

Multicentric, comparative, randomized, open clinical trial. Unani Coded drug *UNIM-904* and amlodipine were obtained from Central Council for Research in Unani Medicine, New Delhi. The study was carried out at Regional Research Institute of Unani Medicine (RRIUM), Aligarh. One hundred two patients, aged 18-65 years of either sex were selected from the lot of patients attending the out patient department (OPD) of the institute following the predesigned inclusive/exclusive criteria. General physical and clinical examination, symptoms regarding to hypertension and the vital parameters like blood pressure and heart rate had also been studied. Patients had been randomly divided into two treatment groups, test and control following block randomization method. Total registered cases in trial group were 109, completed cases 41 and dropout cases 65. Total registered cases in control group were 114, completed cases 61 and dropout cases 56. The efficacy and safety of Unani coded drug *UNIM-904* and amlodipine were evaluated on the basis of symptomatic, vital parameters (blood pressure and pulse rate and electrocardiogram (ECG)), biochemical and haematological parameters. This research project is registered in Clinical Trial Registry-India. CTRI number: (TRI/2013/10/004091) (registered on 23/10/2013).

Subject selection criteria

Patients were enrolled on the basis of following inclusion and exclusion criteria:

Inclusion criteria

Patients of either sex in the age group of 18-65 years, patients of hypertension with SBP 160-179 mmHg and DBP 90-100 mmHg, presence of any of the following symptoms and signs *viz*; Headache (*suda*), vertigo (*duwar*), palpitation (*khafqan*), laziness (*kasal*), anxiety (*qalaq*), breathlessness (*usr al-tanaffus*), diminished alertness (*takaddur fi'l hawas*), subconjunctival haemorrhage (*jiryan al-dam zer multahima*), epistaxis (*ru'af*), pulsus plenus (*nabz mumtali*), were included.

Exclusion criteria

Patient with SBP ≥180 mmHg and diastolic BP >100 mmHg and secondary hypertension, pregnant and lactating women, females using oral contraceptive pills regularly, patients taking any other medication affecting blood pressure like NSAIDs, patients with abnormality in investigations done at baseline (SGPT >105 IU). Obese subjects – BMI >30, patients with disorders requiring long term-treatment, e.g., diabetes mellitus, drug addicts, alcoholics /malignancy /epilepsy /CAD/CKD, patients with sinus bradycardia, i.e., pulse rate less than 60/min, were excluded.

Drug, Dose and mode of administration

The trial Unani coded drug *UNIM-904* was given orally to the patients in the form of sachet in a dose of 5.0 gm granules twice a day before 30 minutes of lunch and dinner and control allopathic drug amlodipine was given orally in a dose of one tablet (5 mg) once a day to the patients for a period of 12 weeks-days.

Assessment of temperament (*mizaj*)

Assessment of temperament (*mizāj*) has been done at baseline.

1. Criteria for assessment of efficacy

Reduction in systolic and diastolic blood pressure. Improvement observed in the following signs and symptoms of essential hypertension *viz*; Headache (*suda*), vertigo (*duwar*), palpitation (*khafqan*), laziness (*kasal*), anxiety (*qalaq*), breathlessness (*usr al-tanaffus*), diminished alertness (*takaddur fi'l hawas*), subconjunctival haemorrhage (*jiryan al-dam zer multahima*), epistaxis (*ru'af*) and pulsus plenus (*nabz mumtali*). All the signs and symptoms have been graded on a 10 point visual analog scale (VAS).

2. Criteria for assessment of safety

Biochemical studies

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

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) [21], serum alkaline phosphatase enzyme (S-ALP, EC. 3.1.3.1) by the method of Wilkinson *et al* (1969) [22], blood urea by the method of Tiffany *et al.* (1972) [23], serum creatinine by Bowers (1980) method [24], serum total bilirubin by modified method of Pearlman & Lee (1974) [25], uric acid by modified Trinder peroxidase Method [26], cholesterol by modified Roeschlau's method [27], triglycerides by Fossati *et al*, (1969) [28], HDL by Burstein *et al*, (1970) [29], calcium by method of Moorehead and Briggs (1974) [30], sodium and potassium by electrolyte analyzer (2014) [31].

Haematological studies

Haematological parameters were done [32]. 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 various biochemical parameters.

3. Statistical analysis

Data were analyzed statistically by 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

1. Demographic Study

In trial group, out of 41 patients of essential hypertension 16 (39.02%) were male and 25 (60.98%) female, whereas in control group, 19 (31.15%) were male and 42 (68.85%) female, which shows that females have higher incidence as compared to male. Similar conclusion had been reported by other workers [33]. In both trial as well as control group of females with age group 41-65 years were 18 (43.90%) and 29 (47.54%) respectively, have higher incidence followed by age group 11-40 years 07 (17%) and 13 (21.31%) respectively (table-1). Risk factors comprise of family history, body mass index (BMI), smoking, tobacco chewing and alcohol intake. In both trial and control group, 02 (4.88%) and 01 (1.64%) of patients respectively had family history of hypertension. In both trial and control group of female subjects 24 (58.54%) and 42 (68.85%) (table-1) respectively had greater BMI than 25 kg/m^2, whereas males of both the groups 17 (41.46%) and 19 (31.15%) had greater BMI than $\geq$25 kg/m^2. There was an association between body mass index and hypertension [34]. In control group 01 (1.64%) of patient had smoking habits, whereas in both trial and control groups 05 (12.20%) and 02 (3.28%) (table-1) of patients respectively had tobacco chewing habit. Some authors had reported earlier that there was an association between cigarette smoking, and blood pressure [35]. In dietary habits of both trial and control group, non-vegetarian 35 (85.37%) and 54 (88.53%) had more incidence than vegetarian 06 (14.63%) and 07 (11.29%) (Table-1) respectively. Similar conclusion had been reported by other workers [36]. In assessment of temperament (mizaj) of both trial (UNIM-904) and control (amlodipine) group, the higher incidence was found in phlegmatic (balghami) 41 (100%) and 61 (100%) temperament respectively (table-1).

Safety measurement

Effect on liver and kidney function tests

Biochemical studies undertaken have indicated that there were no significant changes in liver function tests as well as kidney function tests. Therefore, it can be inferred that the test drug *UNIM-904* did not induce any negative or unfavorable response. The safety of the drug is therefore conformed (Table-8).

Clinical studies

Assessment of efficacy

When one group of Unani coded drug *UNIM-904* in the form of sachet of 5.0 gm whereas other group, one tablet of amlodipine (5.0 mg) were given to patients orally with water twice a day before 30 minutes of meals for a period of 12 weeks respectively, in both the groups, the effected changes in various hypertensive patient's signs and symptoms were recorded and follows as under:

1. Subjective parameters

i. Headache

A significant reduction in score 27.78% (P<0.0001)) on 1st –week, 38.62% (P<0.0001), 2nd -week 48.41% (P<0.0001) 3rd week, 57.41% (P<0.0001) 4rth week, 74.07% (P<0.0001) 6th and 8th week, 83.33% (P<0.0001) 10th week and 76.46% (P< 0.0001) 12th week and 3.29% (P< 0.0001) on 1st –week, 25.45% (P< 0.0001) 2nd –week, 44.91% (P< 0.0001) 3rd week, 57.19% (P< 0.0001) 4rth week, 59.89% (P< 0.0001) 6th and 8th week, 69.16% (P< 0.0001) 10th week and 79.34% (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 and fig-2). Similar observations had been reported by other authors [37, 38].

ii. Vertigo

A significant reduction in score 12.04% (P<0.0001)) on 1st –week, 35.19% (P<0.0001) 2nd –week, 46.61% (P<0.0001) 3rd week, 57.10% (P<0.0001) 4rth week, 70.68% (P<0.0001) 6th and 8th week, 84.26% (P<0.0001) 10th week and 90.12% (P<0.0001) 12th week whereas 20.96% (P<0.0001) on 1st –week, 33.83% (P<0.0001) 2nd –week, 44.61% (P<0.0001) 3rd week, 64.67% (P<0.0001) 4rth week, 62.58% (P<0.0001) 6th and 8th week, 74.55% (P<0.0001) 10th week and 83.83% (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 and fig-2).Similar observations had been reported by other workers [37, 38].

iii. Palpitation

A significant reduction in score 15.16% (P<0.0001)) on 1st –week, 44.84% (P<0.0001) 2nd –week, 65.48% (P<0.0001) 3rd week, 73.23% (P<0.0001) 4th-week, 83.55% (P<0.0001) 6th and 8th-week, 89.68% (P<0.0001) 10th-week and 95.16% (P<0.0001) 12th-week whereas 31.41% (P<0.0001) on 1st-week, 42.60% (P<0.0001) 2nd-week, 45.49% (P<0.0001) 3rd-week, 62.82% (P<0.0001) 4th-week, 67.87% (P<0.0001) 6th and 8th-week, 86.28% (P<0.0001) 10th-week and 91.70% (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 and fig-2).Similar observations had been reported by other workers [37, 38].

iv. Laziness

A significant reduction in score 37.90% (P<0.0001) on 1st –week, 61.05% (P<0.0001) 2nd –week, 74.74% (P<0.0001) 3rd-week, 94.74% (P<0.0001) 4-week, 82.11% (P<0.0001) 6th, 8th and 10th-week, and 100.00% (P<0.0001) 12th-week whereas 37.27% (P<0.0001)) on 1st-week, 49.10% (P<0.0001) 2nd-week, 67.27% (P<0.0001) 3rd and 4th-week, 81.82% (P<0.0001) 6th and 8th and 10th-week, and 97.27% (P<0.0001) 12th-week whereas respectively had been observed, and these were compared with the values of baseline and different follow-up of treatment (Table-2,3 and fig-2).Similar observations had been reported by other workers [37, 38]. No significant change in anxiety, breathlessness and diminished alertness had been observed.

v. Assessment of blood pressure

a. Effect on systolic blood pressure

A significant reduction in female systolic blood pressure 1.89% (P<0.01) on 1st -week, 5.03% (P<0.0001) 2nd-week, 10.69% (P<0.0001) 3rd, 4th and 6th-week 13.21% (P<0.0001) 8th-week, 13.84% (P<0.0001) 10th-week, and 16.98% (P<0.0001) 12th-week whereas 3.17% (P<0.0001)) on 1st-week, 6.33% (P<0.0001) 2nd-week, 9.49% (P<0.0001) 3rd and 4th- week, 11.39% (P<0.0001) 6th and

8th-week 12.66% (P<0.0001) 10th-week, and 13.92% (P<0.0001) 12th-week respectively had been observed. A significant reduction in male systolic blood pressure 2.50% (P<0.05) on 1st-week, 5.63% (P<0.0001) 2nd-week, 7.50% (P<0.0001) 3rd-week, 8.75% (P<0.0001) 4th-week 9.38% (P<0.0001) 6th-week, 10.63% (P<0.0001) 8th-week, 10.00% (P<0.0001) 10th-week, and 11.25% (P<0.0001) 12th-week whereas 4.94% (P<0.01)) on 1st-week, 5.56% (P<0.01) 2nd-week, 8.64% (P<0.0001) 3rd-week, 9.88% (P<0.0001) 4th-week, 10.49% (P<0.0001) 6th-week, 14.20% (P<0.0001) 8th-week and 10th-week and 15.43% (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 and fig-1). Similar observations had been reported by other workers [39, 40].

b. Effect on diastolic blood pressure

A significant reduction in female diastolic blood pressure 4.26% (P<0.05) on 1st-week, 8.51% (P<0.05) 2nd-week, 11.70% (P<0.0001) 4th-week, 12.77% (P<0.0001) 6th-week, 17.02% (P<0.0001) 8th-week, 13.83% (P<0.0001) 10th-week, and 15.96% (P<0.0001) 12th-week whereas 8.60% (P<0.01) 3rd-week, 11.83% (P<0.0001) 4th-week, 13.98% (P<0.0001) 6th-week, 15.05% (P<0.0001) 8th and 10th-week, and 17.20% (P<0.0001) 12th-week respectively had been observed. A significant reduction in male diastolic blood pressure 7.27% (P<0.01) 2nd-week, 9.38% (P<0.01) 3rd-week, 11.46% (P<0.0001) 4th-week, 13.54% (P<0.0001) 6th-week, 12.50% (P<0.0001) 8th-week, 11.46% (P<0.0001) 10th week, and 15.63% (P<0.0001) 12th-week whereas 8.25% (P<0.01)) on 1st-week, 11.34% (P<0.0001) 2nd-week, 14.43% (P<0.01) 3rd-week, 15.46% (P<0.0001) 4th-week, 16.50% (P<0.0001) 6th-week and 8th-week, 20.62% (P<0.0001) 10th-week and 12th-week respectively had been observed and these were compared with the values of baseline and different follow-up of treatment (Table-2, 3 and fig-1). Similar observations had been reported by other workers [39, 40].

c. Effect on pulse rate

A significant reduction in female pulse rate 4.26% (P<0.05) on 1st-week, 8.51% (P<0.01) 2nd-week, 11.70% (P<0.0001) 4th-week, 12.77% (P<0.0001) 6th-week, 17.02% (P<0.0001) 8th-week, 13.83% (P<0.0001) 10th-week, and 15.96% (P<0.0001) 12th-week whereas 3.70% (P<0.05) 2nd-week, 3rd and 4th-week, 4.94% (P<0.0001) 6th, 8th and 10th-week, 6.17% (P<0.0001) 12th-week, respectively had been observed. A significant reduction in male pulse rate 7.29% (P<0.01) 2nd-week, 9.38% (P<0.01) 3rd-week, 11.46% (P<0.0001) 4th and 10th-week, 13.54% (P<0.0001) 6th-week, 12.50% (P<0.0001) 8th-week, 15.63% (P<0.0001) 12th-week whereas 3.70% (P<0.05)) on 2st-week, 4.94% (P<0.01) 3rd, 4th- and 6th-week, 6.17% (P<0.0001) 8th-week, 3.70% (P<0.0001) 10th-week and 8.64% (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 and fig-1). Similar observations had been reported by other workers [39, 40].

d. Effect on Electrocardiogram

No changes in electrocardiogram had been observed.

3. Objective parameters

a. Effect on lipid and electrolyte profiles

No significant changes in lipid (cholesterol, triglycerides and HDL) and electrolyte (sodium, potassium and calcium) profile respectively had been observed (Table-7) in both UNIM-904 and amlodipine treated patients after 12 weeks.

b. 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) in both UNIM-904 and amlodipine treated patients after 12 weeks.

Table 1: Demographic data showing the distribution of different variables of trial and control group of hypertensive patients

Vaiables ↓ Group →	Sex	Trial group %age n=41	Mean age ± S.D	Control group %age, n= 61	Mean age ± S.D
1. Sex wise	Female	25 (60.98%)	47.96±8.96	42 (68.85%)	45.55±9.65
	Male	16 (39.02%)	48.88±10.16	19 (31.15%)	48.63±11.64
2. Age-wise (yrs) i. 10-20	Female	Nil		Nil	
	Male	Nil		Nil	
ii. 21-40	Female	07 (17.00%)		13 (21.31%)	
	Male	03 (7.32%)		13 (21.31%)	
iii.41-65	Female	18 (43.90%)		29 (47.54%)	
	Male	13 (31.71%)		06 (9.84%)	
3. Risk factors i. Body mass index (Kg/M^2)	Female	24 (26.71±1.09)		42 (26.74±0.75)	
	Male	17 (28.80 ±1.91)		19 (26.81±0.54)	
ii. Family history		02 (4.88%)		01 (1.64%)	
iii. Smoking		Nil		01 (1.64%)	
iv. Tobacco chewing		05 (12.20%)		02 (3.28%)	
v. Alcoholic		Nil		Nil	
4. Dietary habits i. Non-vegetarian		35 (85.37%)		54 (88.53%)	
ii. Vegetarian		06 (14.63%)		07 (11.29%)	
5.Assessment of temperament (mizaj) i. Phlegmatic (balghami)		41 41 (100.00%)		61 61 (100.00%)	
ii. Bilious (safrawi)		Nil		Nil	
iii. Sanguine (damavi)		Nil		Nil	
iv. Melancholic (Sawdawi)		Nil		Nil	

Table 2: Comparative data showing improvement of various signs and symptoms of hypertensive patients treated with Unani coded drug *UNIM-904* and allopathic drug amlodipine.

Group↓	Parameter → Symptom↓	BL (1st-day)	1st F-up (1st-wk)	2nd F-up (2nd-wk)	3rd F-up (3rd-wk)	4th F-up (4th-wk)	5th F-up (6th-wk)	6th F-up (8th-wk)	7th F-up (10th-wk)	8th F-up (12th-wk)
UNIM-904	Headache	3.78 ±1.49	2.73 ±1.75***	2.32 ±16.20***	1.95 ±1.60***	1.61 ±1.43***	0.98 ±1.19***	0.98 ±1.19***	0.63 ±0.94***	0.89 ±0.93***
Amlodipine	Headache	3.34 ±1.61	3.23 ±1.44***	2.49 ±1.65***	1.84 ±1.54***	1.43 ±1.44***	1.34 ±1.12***	1.34 ±1.12***	1.03 ±1.26***	0.69 ±0.96***
UNIM-904	Vertigo	3.24 ±1.56	2.85 ±1.68***	2.10 ±1.64***	1.73 ±1.60***	1.39 ±1.39***	0.95 ±1.18***	0.95 ±1.18***	0.51 ±0.90***	0.32 ±0.72***
Amlodipine	Vertigo	3.34 ±1.72	2.64 ±1.65***	2.21 ±1.59***	1.85 ±1.60***	1.18 ±1.18***	1.25 ±1.27***	1.25 ±1.27***	0.85 ±1.12***	0.54 ±0.89***
UNIM-904	Khafaqan	3.10 ±1.61	2.63 ±1.70***	1.71 ±1.62***	1.07 ±1.19***	0.83 ±1.14***	0.51 ±0.98***	0.51 ±0.98***	0.32 ±0.85***	0.15 ±0.53***
Amlodipine	Khafaqan	2.77 ±1.62	1.90 ±1.42***	1.59 ±1.42***	1.51 ±1.51***	1.03 ±1.21***	0.89 ±1.29***	0.89 ±1.29***	0.38 ±0.82***	0.23 ±0.74***
UNIM-904	Laziness	0.95 ±1.38	0.59 ±1.02**	0.37 ±0.99**	0.24 ±0.66***	0.05 ±0.31***	0.17 ±0.54***	0.17 ±0.54***	0.17 ±0.54***	Nil
Amlodipine	Laziness	1.10 ±1.39	0.69 ±1.09***	0.56 ±1.10***	0.36 ±0.76***	0.36 ±0.76***	0.20 ±0.60***	0.20 ±0.60***	0.20 ±0.60***	0.03 ±0.26***
UNIM-904	Anxiety	0.10 ±0.44	0.20 ±0.60•	0.05 ±0.31•	Nil	Nil	0.05 ±0.31•	0.05 ±0.31•	0.05 ±0.31•	0.05 ±0.31•
Amlodipine	Anxiety	0.03 ±0.26	0.13 ±0.50•	0.20 ±0.70•	0.03 ±0.26•	0.03 ±0.26•	0.10 ±0.77•	0.10 ±0.77•	0.03 ±0.26•	Nil
UNIM-904	Breathlessness	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Amlodipine	Breathlessness	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
UNIM-904	Diminished alertness	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Amlodipine	Diminished alertness	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

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

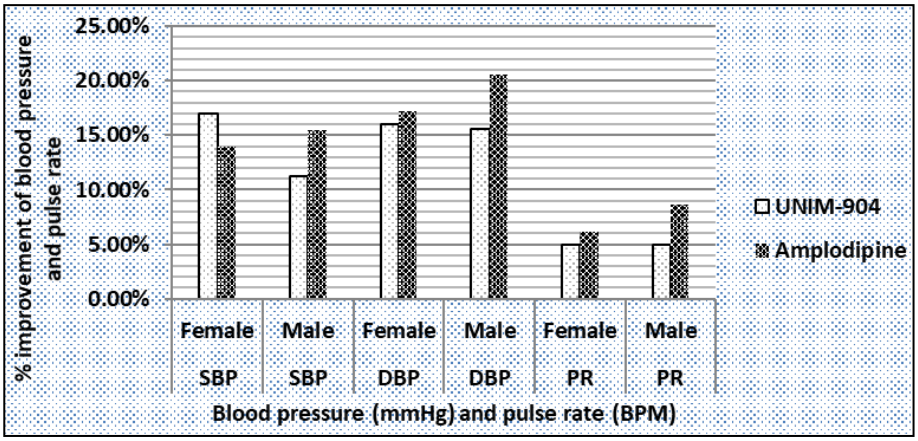

Fig 1: Comparative data showing improvement in blood pressure and pulse rate in hypertensive patients under trial (UNIM-904) and control group (amlodipine).

Table 3: Comparative data showing improvement in symptoms of hypertensive patients in trial and control groups.

S. No	Name of symptom	UNIM-904	Amlodipine
1	Headache	76.45%	79.34%
2	Vertigo	92.90%	83.83%
3	Palpitation	95.16%	91.70%
4	Laziness	100.0%	97.27%
5	Anxiety	100.0%	100.0%

Table 4: Comparative data showing improvement in blood pressure (systolic and diastolic) and pulse rate of hypertensive females and males patients treated with UNIM-904 and allopathic drug amlodipine

Group↓	Parameter ↓	BL (1st-day)	1st F-up (1st-wk)	2nd F-up (2nd-wk)	3rd F-up (3rd-wk)	4th F-up (4th-wk)	5th F-up (6th-wk)	6th F-up (8th-wk)	7th F-up (10th-wk)	8th F-up (12th-wk)
UNIM-904	Female SBP n=24	159.0 ±3.92	156.0 ±4.78**	151.0 ±6.55***	141.0 ±12.62***	141.0 ±7.08***	141.0 ±7.50***	138.0 ±10.60***	137.0 ±11.27***	132.0 ±9.17***
Amlodipine	Female SBP n=42	158.0 ±8.82	153.0 ±9.39**	148.0 ±9.93***	143.0 ±11.46***	143.0 ±8.33***	140.0 ±7.41***	140.0 ±8.94***	138.0 ±8.45***	136.0 ±8.22***
UNIM-904	Male SBP n=17	160.0 ±4.65	156.0 ±7.94*	151.0 ±7.75**	148.0 ±6.94***	146.0 ±9.43***	145.0 ±10.87***	143.0 ±11.07***	144.0 ±11.94***	142.0 ±11.73***

Amlodipine	Male SBP n=19	162.0 ±5.93	154.0 ±6.99**	153.0 ±9.54**	148.0 ±6.41***	146.0 ±10.05***	145.0 ±8.28***	139.0 ±13.19***	139.0 ±9.14***	137.0 ±9.77***
UNIM-904	Female DBP n=24	94.0 ±5.51	90.0 ±6.85*	86.0 ±7.08**	90.0 ±18.33	83.0 ±6.11***	82.0 ±6.23***	78.0 ±8.56***	81.0 ±9.34***	79.0 ±6.37***
Amlodipine	Female DBP n=42	93.0 ±4.45	89.0 ±5.38	84.0 ±5.94	85.0 ±14.15**	82.0 ±6.00***	80.0 ±6.23***	79.0 ±4.51***	79.0 ±5.31***	77.0 ±6.02***
UNIM-904	Male DBP n=17	96.0 ±5.09	93.0 ±5.98	89.0 ±9.08**	87.0 ±8.44**	85.0 ±8.58***	83.0 ±7.32***	84.0 ±9.26***	85.0 ±10.58***	81.0 ±6.00***
Amlodipine	Male DBP n=19	97.0 ±4.67	89.0 ±7.47**	86.0 ±7.30***	83.0 ±6.97**	82.0 ±7.47***	81.0 ±6.32***	81.0 ±11.07***	77.0 ±5.33***	77.0 ±7.21***
UNIM-904	Female PR n=24	94.0 ±5.51	90.0 ±6.8[5]*	86.0 ±7.08**	90.0 ±18.33	83.0 ±6.11***	82.0 ±6.23***	78.0 ±8.56***	81.0 ±9.34***	79.0 ±6.37***
Amlodipine	Female PR n=42	81.0 ±5.54	80.0 ±12.30	78.0 ±4.70*	78.0 ±5.76*	78.0 ±3.78**	77.0 ±2.46***	77.0 ±2.61***	77.0 ±2.88***	76.0 ±2.79***
UNIM-904	Male PR n=17	96.0 ±5.09	93.0 ±5.98	89.0 ±9.08**	87.0 ±8.44**	85.0 ±8.58***	83.0 ±7.32***	84.0 ±9.26***	85.0 ±10.58***	81.0 ±6.00***
Amlodipine	Male PR n=19	81.0 ±6.07	78.0 ±3.19	78.0 ±4.60*	77.0 ±2.63*	77.0 ±3.95**	77.0 ±3.40***	76.0 ±2.58***	78.0 ±4.64***	74.0 ±6.60***

SBP= Systolic blood pressure (mm Hg), DBP= Diastolic blood pressure (mm Hg), PR= Pulse rate, BPM= Beats per minute [*P<0.05, **P<0.01 are significant, ***P<0.001 is highly significant and 'P is not significant]

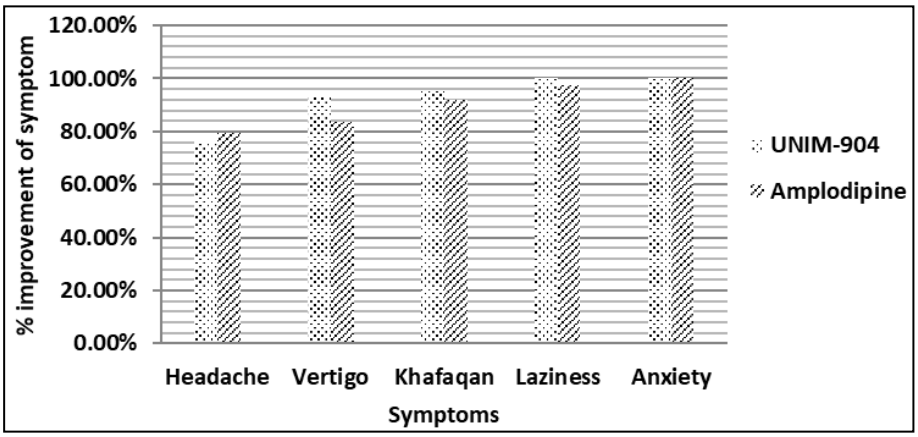

Fig 2: Comparative data showing improvement in symptoms in hypertensive patients under trial (UNIM-904) and control group (amlodipine)

Table 5: Comparative data showing improvement in blood pressure and pulse rate in hypertensive patients of trial and control group.

S. No	Blood pressure ↓ Group →		UNIM-904	Amlodipine
1	Systolic (mmHg)	Female	16.98%	13.92%
		Male	11.25%	15.43%
2	Diastolic (mmHg)	Female	15.96%	17.20%
		Male	15.63%	20.62%
3	Pulse rate (BPM) (bpm)	Female	5%	6.17%
		Male	5%	8.64%

Table 6: Comparative effect of Unani coded drug UNIM-904 and amlodipine in the levels of SGPT, SGOT, alkaline phosphatase, bilirubin, blood urea nitrogen (BUN), serum creatinine, uric acid, in hypertensive 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-904	Baseline (1st -day)	21.18 ±9.68	22.62 ±13.02	87.93 ±45.56	0.74 ±0.21	12.58 ±7.98	1.01 ±0.21	5.24 ±1.60
	2nd follow-up (2nd -week)	23.33 ±9.43'	22.69 ±10.14'	77.09 ±25.81'	0.75 ±0.19'	12.02 ±5.19'	0.99 ±0.20'	5.31 ±1.34'
	8th F-up (12th-week)	25.55 ±12.80'	30.74 ±21.74'	85.22 ±34.65'	0.76 ±0.23'	11.90 ±4.49'	0.97 ±0.19'	5.42 ±1.45'
Amlodipine	Baseline (1st -Day)	24.97 ±9.51	25.00 ±1.77	85.30 ±20.09	0.77 ±0.21	12.14 ±5.72	0.92 ±0.14	4.99 ±1.25
	2nd follow-up (2nd -week)	25.12. ±11.18'	24.53 ±10.56'	87.86 ±20.36'	0.75 ±0.23'	11.47 ±5.75'	0.98 ±0.20'	4.73 ±1.29'
	8th F-up (12th-week)	25.50 ±9.90'	26.30 ±11.36'	86.41 ±22.54'	0.73 ±0.19'	11.60 ±4.43'	0.95 ±0.18'	4.77 ±1.45'

['P is not significant]

Table 7: Comparative effect of Unani coded drug UNIM-904 and amlodipine in the levels of lipid profile (cholesterol triglycerides and HDL) and electrolyte profile (sodium, potassium and calcium) in hypertensive patients.

Parameter ↓ Group →		Cholesterol (mg%)	Triglycerides (mg%)	HDL (gm%)	Sodium m Mol/L	Potassium m Mol/L	Calcium mg/L
UNIM-904	Baseline (1st -day)	174.08 ±31.77	141.78 ±63.09	35.74 ±11.18	138.52 ±10.16	4.68 ±0.34	9.03 ±2.51
	2nd follow-up (2nd -week)	175.03 ±37.97˙	132.14 ±48.00˙	35.47 ±9.69˙	139.83 ±8.40˙	4.68 ±0.41˙	9.40 ±2.44˙
	8th F-up (12th-week)	173.76 ±33.69˙	126.76 ±52.24˙	40.00 ±14.67˙	136.14 ±9.99˙	4.67 ±0.40˙	8.97 ±2.33˙
Amlodipine	Baseline (1st -day)	183.28 ±36.97	127.09 ±51.52	38.26 ±11.11	136.97 ±11.23	4.68 ±0.48	8.69 ±2.60
	2nd follow-up (2nd -week)	178.26 ±38.26˙	119.53 ±34.59˙	37.94 ±10.54˙	137.09 ±7.82˙	7.16 ±18.80˙	8.65 ±2.58˙
	8th F-up (12th-week)	180.69 ±34.09˙	118.47 ±41.74˙	39.40 ±10.52˙	137.88 ±7.26˙	4.60 ±0.40˙	9.40 ±2.53˙

[˙P is not significant]

Table 8: Comparative effect of Unani coded drug UNIM-904 and allopathic drug amlodipine in the levels of haemoglobin, R.B.C. count, total leucocyte counts (TLC), erythrocyte sedimentation rate (ESR), platelets count, prothrombin time, polymorphs, lymphocytes and eosinophils count in hypertensive patients.

Parameter → Group ↓		Haemoglobin (gm%)	RBC (10^6 /mm^3	TLC (10^3/mm^3)	E.S.R. (mm /hr)		Platelet counts (lac/mm^3)	Prothrombin time (Sec.)	Differential leucocyte counts (DLC)		
					1 Hr	2 Hr			Polymorphs (%)	Lymphocytes (%)	Eosinophils (%)
UNIM-904	Baseline (1st -day)	12.91 ±1.36	4.34 ±0.47	7.82 ±2.32	37.00 ±11.57	45.00 ±10.72	2.41 ±1.59	13.59 ±4.55	67.00 ±8.65	28.00 ±8.19	5.0 ±1.87
	2nd f-up (2nd-week)	12.66 ±1.42˙	4.30 ±0.51˙	7.91 ±2.47˙	37.00 ±12.47˙	46.00 ±10.59˙	2.38 ±1.49˙	12.82 ±3.89˙	66.00 ±7.41˙	29.00 ±7.52˙	5.0 ±2.11˙
	8th F-up (12th-week)	12.68 ±1.60˙	4.30 ±0.52˙	8.07 ±2.74˙	35.00 ±13.39˙	44.00 ±11.36˙	2.31 ±1.42˙	11.77 ±3.19˙	70.00 ±8.27˙	26.00 ±7.94˙	4.0 ±2.13˙
Amlodipine	Baseline (1st -day)	12.46 ±1.54	4.23 ±0.48	7.73 ±2.05	39.00 ±11.95	48.00 ±9.84	2.14 ±0.61	13.02 ±3.56	66.00 ±9.30	29.00 ±8.98	5.0 ±1.74
	2nd F-up (2nd-week)	12.44 ±1.57˙	4.27 ±0.55˙	7.91 ±2.28˙	38.00 ±13.55˙	47.00 ±11.20˙	2.25 ±0.67˙	12.42 ±2.86˙	66.00 ±7.30˙	29.00 ±8.28˙	5.0 ±1.80˙
	8th F-up (12th-week)	12.64 ±1.53˙	4.34 ±0.53˙	7.63 ±2.27˙	40.00 ±10.87˙	49.00 ±9.11˙	2.15 ±0.65˙	11.82 ±2.32˙	69.00 ±9.38˙	26.00 ±9.05˙	5.0 ±2.19˙

[˙P is not significant]

Conclusion

The present study concludes that Unani coded drug UNIM-904 is effective and safe in hypertensive patients and drastically reduces major symptoms *viz*, vertigo, palpitation and laziness as compared to allopathic drug amlodipine (table 3 and fig-2). We, therefore, recommend this drug for further investigations on a larger group of patients with a view to develop a viable herbal drug of choice to combat hypertension, a disease thus far, eluding satisfactory cure in modern medicine.

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