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Effect of a polyherbal Unani formulation on chronic urticaria

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The present study was carried out in the Clinical Research Unit of Majeedia Hospital, Jamia Hamdard, New Delhi during 1996-1998. The aim and objective of the study was to develop safe and effective treatment of urticaria from herbal sources. In this double blind study, patients of chronic urticaria were randomly allocated to receive either *Pitkirya*, a poly herbal formulation or placebo, two capsules daily for 4 weeks. *Pitkirya* treatment significantly reduced all the symptoms of chronic urticaria without producing any serious side effects. Statistically significant difference was found between the results of *Pitkirya* and placebo, *Pitkirya* was found to be much superior over the placebo. Clinical and laboratory parameters showed the efficacy and safety of *Pitkirya,* which was found to be highly effective and safe drug for the treatment of urticaria.

Key words: Unani medicine, Urticaria, *Pitkirya*, Unani system of medicine
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Urticaria is a common condition affecting 15-20% population on at least one occasion[1,2]. It is a focal oedema of the dermis due to a transient increase in capillary permeability[3]. Urticaria may appear as cutaneous manifestations of localized non-pitting oedema usually surrounded by an area of erythema[3,4]. Lesions of urticaria can involve any part of the skin and appear in crops of 24 to 72 hrs duration, with old lesions fading as new ones appear[4].

Ancient Unani physicians have described this disease by the name of *Shara*[5,] commonly known as *Pitti* and *Chhapaki*. According to Unani literature, *Shara* is a disease of skin, which is caused by *Fasad-e-Dam* (disorder of blood). Excessive amount of *Safra* (bile) or *Balgham-e-Shore* (abnormal phlegm) may be the factors for such type of disorder[6,7]. Severe heat of such blood produces weakness of the nerves, which ultimately results in urticaria rashes[8].

The urticaria may be acute or chronic, acute urticaria lasts for less than 6 weeks, whereas chronic urticaria persists over a period of more than 6 weeks[9,10]. The etiology of chronic urticaria remains undetermined in approximately 80 % of cases[5,11]. Therefore, there is an enduring need for symptomatic treatments that are well tolerated, efficacious and safe on long-term use. For the treatment of urticaria different antihistamines and steroids are used in clinical practice. These drugs produce some serious side effects if used for longer duration of time. Moreover, chronic urticaria does not always respond to conventional antihistamine drugs and hence, other drugs are sometimes needed. Considering these facts, present study was planned to develop a safe and effective remedy from herbal sources. The aim of the present study was to evaluate the therapeutic efficacy and safety of a polyherbal Unani formulation in patients of chronic urticaria.

The Unani formulation, *Pitkirya* capsule containing *Asrol* (*Rauwolfia serpentina* Linn.), *Bachh* (*Acorus calamus* Linn.), *Biranjasif* (*Achillea millefolium* Linn.), *Shahtara* (*Fumaria officinalis* Linn.), *Sumbuluttib* (*Nardostachys jatamansi* DC.), *Ustukhuddus* (*Lavandula stoechas* Linn.) was tested clinically for its efficacy and safety in the treatment of urticaria patients.

These drugs have been mentioned as *Musaffi-e-Dam* (blood purifier), *Musakkin* (sedative), *Muhallil-e-Auram* (antiinflammatory), *Mudir* (diuretic), and *Musakkin-e-Asab* (tranquilizer). Different pharmacological actions and other properties of herbal ingredients of *Pitkirya* are as follows:

1. *Asrol* (*Rauwolfia serpentina* Linn.)

It acts as *Musakkin-wo-Munawwim* (sedative and hypnotic)[12,13,14], *Mudir* (diuretic)[15], *Musakkin-e-Asab* (nervine sedative), and *Mukhaddir* (anaesthetic)[12]. Its alkaloid reserpine has antihypertensive activity[14]. In

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Unani System of Medicine, it is used for the treatment of insomnia, melancholia and hypertension[14].

2. *Bachh* (*Acorus calamus* Linn.)

It acts as *Muqawwi-e-Asab* (nervine tonic), Mudir (diuretic), *Qatil-e-Kiram-e-Shikam* (wormicidal)[12], *Dafa-e-Damah* (antiasthmatic)[16] and *Musakkin-e-Alam* (sedative & analgesic)[17]. It is used in the treatment of paralysis, epilepsy, retention of urine, and intestinal worms. It is used as *Qat-e-Balgham* i.e. it removes excessive amounts of phlegm from the body[18]. It is also used for the treatment of various skin disorders[19]. Furthermore, it is used for the treatment of snakebite and scorpion sting[16.]

3. *Biranjasif (Achillea millefolium* Linn.)

Biranjasif acts as *Muhallil-e-Auram* (anti-inflammatory), *Mudir-e-Bol-wo-Haiz* (diuretic & emmenagogue)[12,14,20], *Musakkin-e-Alam* (analgesic), *Daf-e-Humma* (antipyretic), *Muqawwi-e-Dimagh* (brain tonic), *Musaffi Khoon* (blood purifier), *Habis-e-Dam* (haemostatic), and *Hazim* (carminative)[17]. It is used in liver and chest complaints, retention of urine, amenorrhoea, and inflammatory conditions[16]. It is also used as an antidote for scorpion stings[19].

4. *Shahtara (Fumaria officinalis* Linn.)

It acts as *Musaffi Khoon* (blood purifier), *Qatil-e-Kiram-o-Shikam* (anthelmintic)[21], *Mudir* (diuretic), *Mulayyan* (laxative), *Dafa-e-Humma* (antipyretic)[12]. It is used for the treatment of various skin diseases, e.g. eczema, itching, leukoderma. It is also used for the treatment of intestinal worms[19,22].

5. *Sumbuluttib (Nardostachys jatamansi* DC.)

Sumbuluttib acts as *Muqawwi-e-Dimagh* (brain tonic), *Muhallil* (anti-inflammatory), *Dafa-e-Tashannuj* (anticonvulsant), *Muqawwi-e-Aza-e-Raisa* (tonic), *Mudir* (diuretic)[19,23], *Muqawwi-e-Asab* (nervine tonic)[23], *Muqawwi-e-Hafiza* (intellect promoting)[19], *Muqawwi-e-Bah* (aphrodisiac)[23]. It is used for the treatment of inflammatory conditions of visceral organs, jaundice, ascitis[19], nervine pain, epilepsy, hysteria, palpitation, chorea, and amenorrhoea[14]. It is also used to alleviate various skin affections like leprosy and erysipelas. Pharmacological studies of *Sumbuluttib* determined its hypotensive, bronchodilating, tranquilizing, and antibacterial activities. It inhibited the bronchoconstrictor response of histamine[22].

6. *Ustukhuddus (Lavandula stoechas* Linn.)

It acts as *Muqawwi-e-Medah, Jigar-wo-Dimagh* (stomach, liver and brain tonic)[19], *Hazim* (carminative), *Muqawwi-e-Asab* (nervine tonic)[23]. It is used for the treatment of paralysis, epilepsy, chronic cold & cough, sinusitis[22]. It is also used to treat headache and diseases due to the nervine weakness[14].

Methodology

The study was carried out in the Clinical Research Unit of Majeedia Hospital, Jamia Hamdard, New Delhi. The test drug was *Pitkirya* capsule, which contained fine powder of *Asrol* (root), *Bach* (rhizome), *Biranjasif* (leaves & flowers), *Shahtara* (leaves & flowers), *Sumbuluttib* (rhizome), and *Ustukhuddus* (leaves & flowers) in equal quantity and the weight of each capsule was 500 mg. The capsule shells used in this trial were bio-medical capsule shells. Hamdard National Foundation (HNF), Delhi, supplied *Pitkirya* and placebo. Both male and female patients belonging to 18-55 yrs of age with at least 6-month history of clinical manifestations of urticaria were assigned randomly to receive *Pitkirya* and placebo capsules in a double blind fashion. Patients with any cardiac, renal and/or hepatic insufficiency were excluded. Cases with known history of drug allergy, pregnant and lactating women were also excluded. All the patients were investigated clinically as well as by laboratory measures to ascertain diagnosis and rule out other significant pathological conditions.

Urticaria episode of the patient at the time of visit, the number and size of wheals, the severity of itching were evaluated. The severity of each symptom was scored on a 4-point scale from 0 to 3 (0= absent, 1= mild, 2= moderate, 3= severe).

Scale or severity of itching:
0= absent; 1= present, but mild; 2= moderate; 3=severe

Scale for number of wheals:
0= absent; 1= <10; 2= >10; 3=body covered in wheals

Scale for size of wheals:
1= 1.5 cm or less; 2= 1.5 to 2.5 centimeter; 3= > 2.5 cm

All patients were examined on day 0, then after every two weeks for a total period of 12 weeks (4 weeks as a double blind, randomized trial and rest of the 8 weeks as an open label study). By using the

same scale, the patients daily recorded the number and duration of urticaria episode, the number of wheals, their size, and the severity of itching in their self-evaluation notebook (SEN). In order to ascertain diagnosis and safety of the drug, Haemoglobin percentage (Hb%), total leukocyte counts (TLC), differential leukocyte counts (DLC), absolute eosinophil counts (AEC), erythrocyte sedimentation rate (ESR), liver function tests (LFT), and kidney function tests (KFT) were carried out. Pulse and blood pressure monitoring, and records of adverse events reported by the patients were also included in the criteria for safety evaluation.

After randomization, patients received either *Pitkirya* or placebo capsule in the dose of 2 capsules daily (each capsule of 500 mg) for 1-month duration in a double blind fashion. Thereafter, the study was continued as an open perspective trial for further 8 weeks. Clinical and laboratory assessment were scheduled at base line and then after every two weeks till the end of the treatment (12 weeks). The results were analyzed by applying both paired and unpaired student 't' test. A written informed consent was taken from every patient before he / she was inducted in this study.

Results

Total 108 patients were registered in the study; out of them 92 subjects completed the treatment for 4 weeks (50 *Pitkirya* and 42 placebo). The reasons for the drop out (Table 1) and the demographic and clinical characteristics of the study population at the time of inclusion (Table 2) shows that there was no significant difference between the two groups. The results of the trial were analyzed after the groups received 4 weeks treatment (Fig. 1), later on *Pitkirya* treatment was continued (as an open perspective trial) for further 8 weeks and the safety of the drug was evaluated after 3 months treatment. *Pitkirya* treatment significantly improved the clinical symptoms of urticaria as assessed by the mean daily scores of itching, number and size of wheals and the number of urticaria episodes (Table 3). No significant reduction was observed in mean symptoms score in Placebo group (Table 4).

In *Pitkirya* treated group, the mean daily score of itching was decreased from 1.96 ± 0.70 to 1.08 ±0.27 (p<. 001). The mean reduction in number and size of the wheals was calculated 0.92 ±0.79 (p<. 001) and 0.76 ± 0.84 (P<. 001), respectively. Mean score of number of urticaria episode was also diminished from 1.40 ± 0.49 to 0.64 ± 0.48 (p<. 001). These results are summarized in Table 3 & Fig.1. In placebo group, the total reduction in the mean score (mean difference) of itching was 0.09 ± 0.33, whereas 0.07 ± 0.26 was the mean difference for each of the number of wheals, size of wheals and the number of urticaria episodes. All these results were found statistically insignificant

Table 1—Details of drop out cases (N=16)

Reason	*Pitkirya*	Placebo
Inefficacy	1	8
Adverse events	1	0
Unknown	2	4
Total	4	12

N=Number of patients

Table 2—Clinical characteristics at inclusion

Characteristic	*Pitkirya* (N=50)	Placebo (N=42)
Male sex N (%)	23 (46)	16 (38.10)
Female sex N (%)	27 (54)	26 (61.90)
Age (years) mean ± SD	31.26 ± 8.33	29.63 ± 7.53
Mean daily number of urticaria episode mean ± SD	1.28 ± 0.45	1.31 ± 0.46
Duration of illness mean ± SD	2.61 ± 1.99	1.90 ± 2.13
Mean duration (hours) of urticaria episodes mean ± SD	7.31 ± 2.05	7.21 ± 2.15
Daily score of severity of itching mean ± SD	1.96 ± 0.70	1.88 ± 0.83
Daily score of number of wheals mean ± SD	1.94 ± 0.76	1.74 ± 0.70
Mean score of size of wheals mean ± SD	1.84 ± 0.82	1.90 ± 0.82

N= number of patients; % = Percentage; SD = Standard deviation

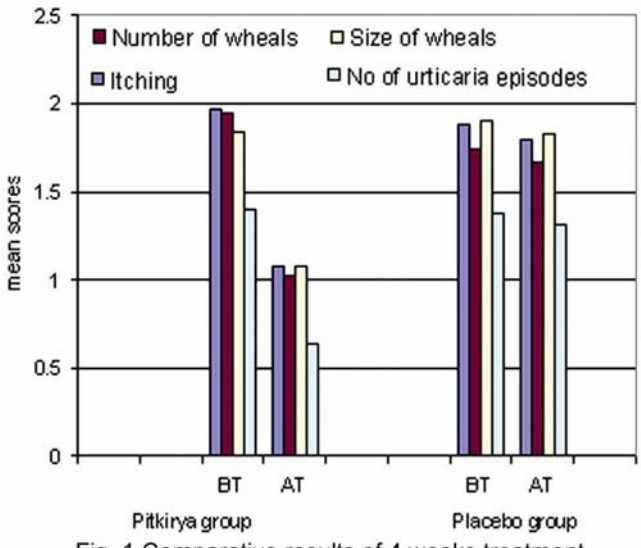

Fig. 1 Comparative results of 4 weeks treatment

Table 3—Results of Pitkirya on different symptoms of urticaria (N=50)

Symptoms	Mean score ± SD		MD	SD of difference	SE of difference	p
	BT	AT				
Itching	1.96 ± 0.70	1.08 ± 0.27	0.88	0.63	0.08	< .001
Number of wheals	1.94 ± 0.76	1.02 ± 0.25	0.92	0.79	0.11	< .001
Size of wheals	1.84 ± 0.82	1.08 ± 0.34	0.76	0.84	.0.12	< .001
Number of urticaria episodes	1.40 ±0.49	0.64 ±0.48	0.76	0.62	0.08	< .001

BT =Before treatment; AT = After treatment; MD = Mean difference; SD = Standard deviation; SE = Standard error; p=Probability of chance

Table 4—Results of Placebo on different symptoms of urticaria (N=42)

Symptoms	Mean score ± SD		MD	SD of difference	SE of difference	p
	BT	AT				
Itching	1.88 ± 0.83	179 ± 0.82	0.09	0.33	0.05	< .10
Number of wheals	1.74 ± 0.70	1.67 ± 0.72	0.07	0.26	0.04	< .10
Size of wheals	1.90 ± 0.82	1.83 ± 0.88	0.07	0.26	0.04	< .10
Number of urticaria episodes	1.38 ± 0.49	1.31 ± 0.56	0.07	0.2 6	0.04	< .10

BT =Before treatment; AT = After treatment; MD = Mean difference; SD = Standard deviation; SE = Standard error; p=Probability of chance

Table 5—Unpaired student 't' test

Symptoms	Mean difference after 4 weeks treatment		Combined variance (SD^2)	SD±	SE ±	p
	Pitkirya	Placebo				
Itching	0.88	0.09	0.24	0.49	0.10	< .001
Number of wheals	0.92	0.07	0.36	0.60	0.12	< .001
Size of wheals	0.76	0.07	0.40	0.63	0.13	< .001
Number of urticaria episodes	0.76	0.07	0.23	0.48	0.09	< .001

SD = Standard deviation; SE = Standard error; p=Probability of chance

(Table 4 & Fig.1). The results of both the treatment were compared statistically by applying unpaired 't' test that proved highly significant difference; the reduction in all the symptoms score was much higher in the *Pitkirya* group as compared with the placebo (p<. 001) (Table 5). *Pitkirya* capsule was found well tolerated and no serious adverse effect was accounted, total 14 patients reported only mild sedation (Table 6). No clinically significant change in pulse and blood pressure was noted, haematological and biochemical tests remained within the normal range during, and after 12-week treatment, which confirmed that the *Pitkirya* was safe even after long-term treatment.

Table 6—Adverse events reported by the patients after *Pitkirya* treatment

Adverse events	Number of patients
Sedation	14
Dizziness	0
Nausea/vomiting	0
Any other	0

Discussion

Pitkirya treatment significantly decreased all the symptoms score in patients of chronic urticaria. Statistically significant difference (p<. 001) was determined between the two groups. *Pitkirya* was proved safe, none of the values of haematological and biochemical laboratory tests were outside the normal range, and no clinically significant adverse effect was observed during and after 12-week *Pitkirya* treatment. It has been demonstrated that antigen-antibody (IgE antibody with specific antigen) reaction results in histamine release from the skin mast cells, which causes urticaria lesions[24]. Hence, the drugs for the treatment of urticaria must hold antihistaminic activity. It is mentioned in classical Unani literature that *Bachh* (*Acorus calamus* Linn.) has anti-asthmatic activity and it is also used as an antidote in snakebite.

By these properties, it can be concluded that *Acorus calamus* may have antihistaminic activity.

Biranjasif (*Achillea millefolium* Linn.) is used for the treatment of scorpion sting; it also possesses the antihistaminic activity. The relief in the symptom of urticaria might be due to the antihistaminic effects of the above two drugs. The drugs *Shahtara* and *Bachh* are known to have wormicidal (anthelmintic) activity, the relief in the symptoms might be due to the anthelmintic activity of these two drugs, as worm infestation frequently causes urticaria[25]. Psychogenic factors, e.g. anxiety, stress play important role in producing urticaria[25]. The tranquilizing and sedative properties of *Sumbuluttib*, *Bachh* and *Asrol* might be additionally helpful in suppressing the psychogenic factors. Blood purifying activity of *Shahtara* and *Biranjasif* might be supportive in providing the relief. *Pitkirya* was found to be safe and very effective drug; the improvement in urticaria symptoms was achieved by combined antihistaminic, anthelmintic, sedative and blood purifying effects of various ingredients of *Pitkirya* capsule. Further investigations and extensive research is required to identify the mechanism of action of this herbal formulation in relation to urticaria.

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