Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2019; 8(4): 84-90
Received: 11-04-2019
Accepted: 15-05-2019

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The clinical study of primary gout and comparative evaluation of Habb-E-Suranjan with allopurinol in its management

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Abstract
Gout (Niqras) involves many aspects of a person's life and increasing prevalence placing a huge burden on Nations health. The study aim was to assess the efficacy and safety of Unani pharmacopoeial formulation Habb-e-Suranjan on primary gouty patients. This was an 18 months, randomized open with Standard control study, carried out on 60 patients (30 Test group+30 Control group) and improvements in subjective parameters were assessed weekly and in objective parameter at the baseline, 15 days and 30 days. The subjective parameters were graded arbitrarily from 0- 3 according to severity in both group. There was a significant improvement in subjective and objective parameters in both groups and no adverse effects were observed during and after trial. Thus, it can be concluded that Habb-e-suranjan and Allopurinol both were significantly effective in resolving the symptoms and signs of gouty arthritis and both have significant effect on reducing serum uric acid level.

Keywords: Allopurinol, gout, Suranjan, unani medicine

1. Introduction
Gout is a metabolic disease that most often affects middle-aged elderly men and postmenopausal women. *Buqrat* (Hippocrates, 460-377 B.C), father of medicine, described gout as "the disease of kings" due to its association with high calorie and protein rich diet and wealthy men who overindulged in food and drinks [1-6]. It results from an increased body pool of urate with hyperuricaemia, which leads to deposition of Monosodium urate (MSU) crystals in joints and other tissue and typically characterized by episodic acute and chronic painful inflammatory gouty arthritis flares [7, 8]. The first metatarsophalangeal joint (podagra) is the initial joint involved in approximately one-half of the patients. When a person has had untreated gout for a long time, more than one joint may be involved including ankle, heels, knees, Achilles tendon, wrists, fingers, and elbows [9, 10].
The persistent hyperuricaemia & untreated patients may develop life-threaten co-morbidities conditions. Such patients are difficult to treat, characterized by frequent flares and persistent inflammation between flares which contribute to joint damage [8]. Hyperuricemia can be result from increased purine uptake, turn-over, production and impaired renal excretion of uric acid or from a combination of the two processes. About 10% of people with hyperuricaemia develop gout, and 80–60% of patients with gout are hyperuricaemic [7, 9, 14].
The prevalence increases substantially with age and increasing serum urate level, affecting around 10% of men and 6% of women over seventy years old[8]. It affects up to 1-2% of men in Western countries and causes mainly disability and poorer quality of life [15]. Ultimate control of gout requires correction of the basic underlying defect: the hyperuracaemia. Normalizing serum uric acid to < 300-360 mol/L (5.0-6.0 mg/dL) is the first step to prevent recurrent attacks, and eliminate tophaceous deposits [9].
According to *Ibn-Hubal* (1122-1233 A.D) and *Hakeem Mohd Hasan Qurshi*, the word *Niqras* is derived from the term '*Naqoroos'* which means 'great toe joint'. Since this disease classically affects the first metatarsophalangeal joint, it has been given this name & majority of the scholars have the same opinion with this assertation [19-26]. *Ali Bin Abbas Majoosi* has asserted that Arthritis when present in the great toe is called Gout or in other words; Gout is the pain and inflammation of great toe [18]. *Ibn-Hubal* also declare that gout affect those persons more who have excess of humors (Akhlat) and their body is unable to excrete, then due to retention, it reaches towards joints and other tissues of body [19].
To combat gout various new drugs were discovered between 1980 & 1990 but allopurinol (Xanthine-oxidase inhibitors) remains the widely used anti-hyperuricaemic drug [5, 32] but it may cause gastric irritation, diarrhea, skin rashes, fever, hepatic and renal dysfunction,

eosinophilia, jaundice and severe liver necrosis, with 20-25% mortality [9, 10]. So, it is the need of time to look forward for better, safe, and low-cost alternative management. Unani system of medicine possesses possible better, safe and low-cost treatment for *Niqras*. Almost all ancient Unani physicians have advocated Habb-e-Suranjan in slowing the progress and relieving the symptoms of *Niqras* [30]. Because of all the above factors the classical pharmacopoeial formulations of Unani system of medicine i. e. Habb-e-Suranjan is tested in present study for its efficacy in halting the progress and relieving the symptoms of gouty arthritis.

2. Material and Methods

This was an 18 months, randomized open with standard control study, approved by Institutional Ethical Committee, conducted on 60 patients (30 Test group+30 Control group) of primary gout visiting the OPD/IPD of Ajmal Khan Tibbiya College and Hospital, Aligarh Muslim University, Aligarh during the period of 2015-2016. Patients fulfilling the inclusion criteria were given the information sheet containing details regarding the nature of study, drug to be used, and method of treatment and if they were agreed, included in the study and asked to sign the informed consent form. The patients were selected on the basis of history, physical examinations, and investigations. A relevant history of each patient was recorded with regard to their chief complaints with duration, name, age; sex, religion, occupation, marital status, food habits and history of use of alcohol were noted down. Other points like family history of gout, history of trauma, renal stone, and acute monoarticular arthritis, history of use of thiazide group of diuretics, and NSAIDs were also meticulously noted down at the commencement of the study. To evaluate the involvement of other system of the body, all patients were interrogated about the presence of dyspnoea, nausea, vomiting, diarrhea, burning micturation, haematuria, proteinuria, frequency of maturation etc. at the commencement of the study (0 day) and thereafter regularly during the follow-up. General physical, systemic, and joints examination of all the patients were recorded regularly in the performa designed for the study. The joint involved were examined for signs of inflamman, active and passive movements and presence of swelling at the beginning of the study (0 day) and thereafter regularly during the follow up i.e. 7^{th} day, 14^{th} day, 21^{st} day, 30^{th} day. The patients were examined for the presence of any tophi too. The hematological assessment of all cases was done at regular intervals. Rheumatoid Arthritis Test (RA-factor) & C - reactive protein (CRP) was carried out at the beginning of the study (0 day) to rule out the presence of rheumatoid disease and LFT, RFT, BSR, haemograme (TLC, DLC, ESR, Hb%) were carried out twice at the beginning of the study (0 day) and then at the end (30 day) to establish the safety & observe the effect (if any) of our drug on renal and liver function and blood sugar. The estimation of serum uric acid was carried out at the beginning of the study (0 day) and then regularly during the follow up at 15^{th} day and 30^{th} day. Temperament of each patient was assessed on the basis of different parameters mentioned in the classical unani literature and treatment period in both study and control group was fixed to 30 days. Diagnosis was made on the basis of ACR criteria (American College of Rheumatology Criteria, satisfying any six of the twelve criteria as recommended).

All the findings were recorded on the case report form designed for the study. A total of 60 patients were randomly allocated into Test & control group respectively, by simple randomization using lottery method. All the observations in both groups were tabulated & statistically analyzed with each other with the help of biostatistician to known which drug is more effective clinically & in reducing the serum uric acid level. The patients who did not fulfill the inclusion criteria were excluded from the study.

The selection of the subjects was made on the basis of following criteria-

2.1 Inclusion criteria

1. Diagnosed case of Hyperuricemia with sign & symptoms of Primary Gout.
2. Age between 30-60 years.
3. Patients of both sexes.
4. Patients able to take part in the study and ready to follow the instructions & sign the informed consent form.

2.2 Exclusion criteria

1. Serious dysfunctions of Renal, Cardiac, Liver & Pulmonary.
2. Pregnancy and Lactation.
3. Secondary Gout.
4. Case aged below 30 years and more than 60 years.

2.3 Withdrawal criteria

1. Failure to consume the drug.
2. Failure to come for follow up.
3. Any adverse drug reaction.

2.4 Method of assessment of the disease

2.4.1 Subjective parameters

Pain
Swelling
Tenderness
Redness over the joints
Increased local temperature in the joints
Painful joints movement.

2.4.2 Objective parameters

Serum Uric Acid level raised beyond the normal limit i.e., more than 7 mg/100ml in males and more than 6mg/100ml in case of females.

2.5 Availability, dosage and mode of administration of test drug & control drug

Habb-e-suranjan is a pharmacopoeial preparation taken from the *Biyaz-e-Kabeer* (Dehli ke Murakkabat) Part II Published by Idara Kitabus shifa New Dehli. This pharmacopoeial formulation is registered for use in gouty arthritis in the country & selected on the basis of conventional Unani Principles of Treatment (*Usool-e-Ilaj*) of Gout, from the list of classical Unani pharmacopoeial preparation. This formulation already being used by the renowned Unani Physicians for the treatment of gouty arthritis for thousands years without any significant side effects. The ingredients of this pill were procured from Dawakhana Tibbiya College AMU, Aligarh. Before preparing the formulation, all the ingredients of the drug i.e. *Aloe barbadensis* (Liliaceae; Sibr Saqootri), *Terminalia chebula* (Combretaceae; Post Halela Zard), *Colchicum autumnale* (Liliaceae; Suranjan Sheerin), was properly identified by an expert to ascertain its originality & purity. After proper identification all the ingredients of drugs were cleaned, taken in equal weight & ground to fine powder to form the pills. Root of *Colchicum autumnale*, Bark of *Terminalia chebula* & dried juice of *Aloe barbadensis*

leaves were use in this formulation. Each patients in the Test group was given Habb-e-suranjan in the dosage of 4 pills (each pills weighing 500 mg) thrice a day orally on empty stomach (6gm/day) irrespective of age, sex, and severity of disease. The control drug Allopurinol (Brand name-Zyloric), was manufactured by *gsk GlaxoSmithKline* Pharmaceuticals Limited Andhra Pradesh India & purchased from the market & 1 tablet of 100 mg was administered orally thrice a day in Control group. The product is also registered in the country to manage the gouty arthritis. Any adverse events or reactions reported by the patients during the study either in test or control group were recorded in the CRF (*Case Report Form*) and severe cases were withdrawn from the study. Clinician choosing the *Habb-e-Suranjan* to treat the gout was trained, licensed & had been practicing medicine for an average of 10 years; and had attended continuing medical education lectures on evidence-based herbal medicine interventions.

2.6 Follow up
Follow up of all the cases were carried out at the baseline, 15 days and 30 days for investigation and weekly for symptomatic relief i.e., at 0,7,14,21, and 30 days.

3. Observation and Results
During the entire course of study, it was observed that the occurrence of disease was higher in Muslims (57%) & male patients (55%) between the age group of 40-60 years (70%). Maximum numbers of patients were married (90%) of middle income group (62%) & had mixed dietary habits (68%), Balghami mizaj (55%) and belonged to housewives group (38%) followed by businessmen 11 cases (18%), servicemen 10 cases (17%), laborers 7 cases (12%), farmer 6 cases (10%), and student 3 cases (5%). Family history, history of attack of monoarticular arthritis, and alcohol addiction was present in 30%, 40% & 10% cases respectively. It was also observed that great toe or first matatarsophalangeal joint was involved in maximum number of cases (42 %), while in 35% cases involvement of joints was polyarticular and knee joint & ankle joint were involved in 15% & 8% cases.

3.1 Effect of drugs on subjective parameters
3.1.1 Painful joints movement
During the study it was observed that painful joints movements were present in all the patient of Test group and 27 patient of Control group. There was improvement in the painful joint movement in 63.33% and 48.14% respectively in Test and Control group. Baseline and 30 day comparison were found to be statically significant (P<0.01) in both test and control groups. To find out more effective drug between Test and control group, Chi Square test has been applied on the data for the difference of Test group and Control group it was found that $\chi^2 = 0.785$ (p = 0.375). This shows that there is no significant difference in both drugs regarding the efficacy. Therefore the effect of both drugs is same on painful joint movement. (Tab. & Graph 1)

Table 1: Effect of drugs on subjective parameters

Features	0 day		7 day		14 day		21 day		30 day	
	No. of patients		No. of patients improved & %		No. of patients improved & %		No. of patients improved & %		No. of patients improved & %	
	T	C	T	C	T	C	T	C	T	C
Painful joints movement	30	27	5 (16.66)	3 (11.11)	9 (30)	6 (22.22)	17 (56.66)	11 (40.74)	19 (63.33)	13 (48.14)
Swelling	21	21	4 (19)	1 (4.76)	7 (33.33)	5 (23.80)	12 (57.14)	9 (42.85)	13 (61.90)	10 (47.61)
Tenderness	24	21	5 (20.83)	2 (9.52)	8 (33.33)	6 (28.57)	10 (41.66)	7 (33.33)	16 (66.66)	12 (57.14)
Increased local temperature	6	5	1 (16.66)	1 (16.66)	2 (33.33)	1 (20)	2 (33.33)	2 (40)	3 (50)	2 (40)
Pain	30	30	6 (20)	3 (10)	10 (33.33)	7 (23.33)	16 (53.33)	11 (36.66)	20 (66.66)	16 (53.33)
p< 0.05 (Paired 't' test applied between zero and 30th day)										

T= Test group (Habb-e-Suranjan), C= Control group (Allopurinol)

3.1.2 Swelling
It was observed that out of 30 patients in each group, 21 patients suffered from swelling in both Test and Control group. There was improvement in the swelling in 61.90% and 47.61% respectively in Test and Control group. Baseline and 30 day comparison were found to be statically significant (P<0.01) in both test and control groups. To find out more effective drug between Test and Control group, Chi Square test has been applied and it was found that χ^2= 0.229 (p = 0.632). This shows that there is no significant difference in both drugs regarding the efficacy. Therefore both treatments have equal effect in the management of swelling. (Tab. & Graph 1)

3.1.3 Tenderness
Out of 30 patients in each group, 24 and 21 patients suffered from swelling in Test and Control group. There was an overall improvement in the tenderness in 66.66% and 57.14% respectively in Test and Control group. Baseline and 30 day comparison were found to be statically significant (P<0.01) in both test and control groups. To find out more effective drug between Test and Control group, Chi Square test has been applied on data and it was found that $\chi^2 = 0.122$ (p = 0.726). This shows that there is no significant difference in both drugs regarding the efficacy. Therefore the effect of both drugs is same on tenderness. (Tab. & Graph 1)

3.1.4 Increased local temperature
Out of 30 patients in Test and Control group, 6 and 5 patients had complaint of increased local temperature. There was an overall improvement in the increased local temperature in 50 % and 40 % respectively in Test and Control group. Baseline and 30 day comparison were found to be statically significant (P<0.01) in both test and control groups. To find out more effective drug between Test and Control group, Chi Square test has been applied on data for the comparison of Test group and control group it was found that $\chi^2 = 0.110$ (p = 0.740). This shows that there is no significant difference in both drugs regarding the efficacy. Therefore both treatments are equally effective in reducing symptom of increased local temperature. (Tab. & Graph 1)

3.1.5 Pain in joints
All the patients in both groups had complaint of pain. The incidence of which gradually fell to 10 and 14 patients respectively in Test and Control group showing an

improvement of 66.66% and 53.33% in Test and Control group respectively. Baseline and 30 day comparison were found to be statically significant ($P<0.01$) in both test and control groups. To find out more effective drug between Test and Control group, Chi Square test has been applied and it was found that $\chi^2 = 0.625$ (p = 0.429). This shows that there is no significant difference in both drugs regarding the efficacy. Therefore both treatments are equally effective in reducing symptom of pain in joints. (Tab. & Graph 1)

3.2 Effect of drugs on objective parameter

The Mean ± SD of serum uric acid before starting the treatment was 8.32±0.96 in Test group and 9.34±1.06 in control group. It got reduced to 7.4±1.01 in Test group and 7.58±1.13 in control group after treatment. On applying paired' test to the observation recorded before and after 30 days of treatment in Test group (t= 11.50, p= 0.01) and in Control group (t= 16.056, p= 0.01). The p value in Test and control group indicates that the effect of both drugs in reducing elevated serum uric acid is significant. To find out more effective drug between Test and Control group, unpaired 't' test has been applied on serum uric acid for the difference of before and after treatment in Test group and before and after treatment in control group and find that t= 0.419, p=0.676. This shows that there is no significant difference in both drugs regarding the efficacy. Therefore both treatments are equally effective in reducing elevated serum uric acid. (Tab. & Graph 2)

Table 2: Effect of drugs on serum uric acid

	Test group			Control group		
	BT	After Treatment		BT	After Treatment	
Follow up in days	0 day	15th days	30th days	0 day	15th days	30th days
Mean Serum uric acid ± S.D. (mg/dl)	8.32 ± 0.96	7.8 ± 1.04	7.4 ± 1.01	9.34 ± 1.06	8.40 ± 1.08	7.58 ± 1.13
	t = 11.50 p=0.01			t = 16.056 p=0.01		

4. Discussion

This clinical study was conducted on 60 patients to evaluate the efficacy of a Test formulation and compare it with the efficacy of control drug in the management of Primary Gout. The disease is predominantly observed in males i.e. 55% and between the age group of 40-60 years, i.e. 70 %. It shows that the gout has an association with sex i.e. male sex and a particular age group i.e. middle age group. Our observations are in accordance with the old description mentioned in classical literature and modern medical text i.e. Gout mainly affects the males and increased incidence and prevalence of gout with age and higher incidence of gout in men than women before menopause and this is due to uricosuric effect of estrogen that suppresses urate levels in premenopausal women [1, 9, 12, 18].

In our study incidence of disease was higher in Muslim and it is because of that disease has an association with the intake of high purine diet (meat and meat products) which is mainly consumed by the Muslims. According to unani physicians and recent literature mentioned in classical modern text book, Purine-rich diet (meat), used by the non-vegetarian, increased the risk of gout. We observed that 32% cases belonged to the vegetarian's diet group and 68% cases belonged to the non-vegetarians diet group, which is similar to recent literatures and description mentioned in classical unani text [1, 3, 9, 16, 17, 32, 35]. In this study out of 60 patients enrolled 90% cases were married and only 10% cases were unmarried. This is accordance with *Buqrat's* saying i.e. "*A young man does not take gout unless he indulges in coitus*". Excessive sexual activity, especially after a meal is recognized as a high risk factor for gout in males [5, 9, 35, 36]. Further studies are needed in this regard. *Avicenna*, *Rhazes* and *Allama Qarshi* have clearly associated phlegm with the pathogenesis of gout. In our observation the phlegmatic temperament were more in numbers (55%), which is similar to description mentioned in classical unani text. [17] It is very clearly mentioned in the classical text book that the disease is related with leisure and rich peoples are commonly affected [1, 16, 17, 18, 32] and it was found that the middle income group particularly of Business and Service class were outnumbered i.e. 62 % and in higher income group it was 15 %. But it is pertinent to mention here that the visitors of our hospital are mainly belonging to lower and middle class, therefore the findings are incoherent. But it is every possibility of trend shift of disease involving more and more to higher middle class and middle class.

Hippocrates recognized the gout as a familial disorder more than 2000 years ago. This assertion is equally relevant even today. Our study included 30% cases having a positive family history, which is consistent with the descriptions given in Oxford Textbook of Rheumatology and Boyd's Pathology?

In the present study only 10% patients had the habit of alcohol consumption, whereas the remaining 90% did not give any such history. This does not coincide with the findings of Choi and colleagues who reported that alcohol consumption is a major triggering factor for gout. This difference can be attributed to two factors. Firstly the small sample size and secondly the higher number of patients included in our study was Muslim. It was observed that 42% cases had the typical presentation of only great toe which is consistent with the description given in standard medical text [1, 3, 9, 12]. This observation may also be a justification for the unani nomenclature (*Niqras*: derived from *Naqaroos* meaning great toe joint) of this disease [17].

To assess the effect of Test and Control drug on subjective parameters the patients were assessed for various sign and symptoms (Painful joints movement, Tenderness, Increased local temperature, Swelling, Redness and Pain). The severity was rated as severe, moderate, mild, and absent and graded as 3, 2, 1, and 0, respectively based on arbitrary grading system. There was significant but gradual improvement observed on every visit of the patient and at the 30th day almost 63.33% and 48.14% patients were noted to be improved in painful joint movement in Test and Control group respectively. Similarly swelling was also improved in 61.90% and 47.61% cases in Test and Control group while 66.66% and 57.14% improvement in tenderness, 50% and 40% improvement in increased in local temperature, 66.66% and 53.33% improvement in pain in joints were noted in Test and Control drug respectively.

Both Test and Control drugs were found to be significance in relieving the symptoms of painful joints movement, tenderness, swelling, increased local temperature, and pain (using paired 't' test, $P<0.01$) but none of the drug is found to be superior to another (using chi square test, $p>0.05$).

These clinical improvements are mainly because of composition of our drug. The relief in pain can be due to the

analgesic activity of *Aloe* [37, 38] and *Colchicum* [39, 40, 42] and Sedative (Musakkin) activity of *Terminalia chebula*[41]. The anti-inflammatory action of *Colchicum* also play a vital role on joint pain and painful joints movement along with reduction in swelling and tenderness and may also be responsible for the response in Test group. The resolving and analgesic action of *Colchicum* is enough to explain the mechanism through which the gradual improvements happened [39, 40, 42].

Colchicum leads to failure of deposition monosodium urate crystals in the joints and cause expulsion of humors causing the disease [39, 40, 43]. *Colchicum* consists of Colchicines which inhibits the aggregation of inflammatory mediators and cytokines on inflammatory sites particularly of synovium and synovial membrane [30].

Aloe due to its strong purgative and mild diuretic properties, *Terminalia* due to its mild diuretic and purgative properties, and *Colchicum* due to its phlegmagogue and mild diuretic properties, facilitates the expulsion of uric acid through the intestine and kidney [16, 17, 27, 28, 35, 37, 38]. Therefore in under excretors, these drugs play a wonderful role. Astringent action as well as tonic action on stomach and intestine of *Terminalia chebula* makes the formulation least toxic [44, 45].

It is therefore *Colchicum* is effective in all inflammatory joint conditions, but due to its excretory action on uric acid, it is mainly prescribed for hyperuricaemia and gouty arthritis, but its purgative action on intestine, astringent and resolving action on joints makes the drug wonderful. This is why the expulsion of uric acid takes place through intestine [28, 42].

Table 2 showing the only objective parameter which was serum uric acid level and it was estimated at 15th day interval, the baseline serum uric acid level was 8.32±0.96 and at the 30th day it was 7.4±1.01 (t=11.50 *P*<0.005) in Test group and the baseline serum uric acid level was 9.34±1.06 and at the 30th day it was 7.58±1.13 (t=16.05 *P*<0.005) in Control group, indicating that both drugs had a very significant action on reducing serum uric acid level.

The well known action of Colchicum i.e. the expulsion of Monosodium urate from the blood and urate crystals from joint affected make the formulation very effective to expel out urate crystals and uric acid through intestine. It is therefore the findings are very much encouraging in the reduction of serum uric acid level. During the study the patients were advised to avoid purine rich diets, encourage taking plenty of water along with our medication.

It was found that drug has no apparent adverse effect on hematological and biochemical parameters during the study and at the end of the study. (Graph 3)

5. Conclusion

it was concluded that Habb-e-suranjan and Allopurinol both were significantly effective in resolving the symptoms and signs of gouty arthritis and both have significant effect on reducing serum uric acid level as well as both has no any adverse effects on safety parameters. Therefore Test drug is safe to use in case of gouty arthritis.

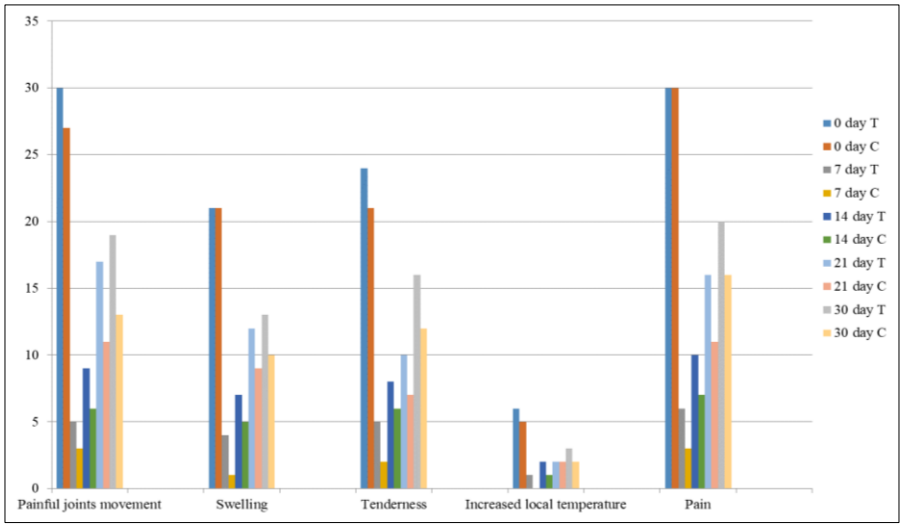

Fig 1: Showing effect of drugs on subjective parameters

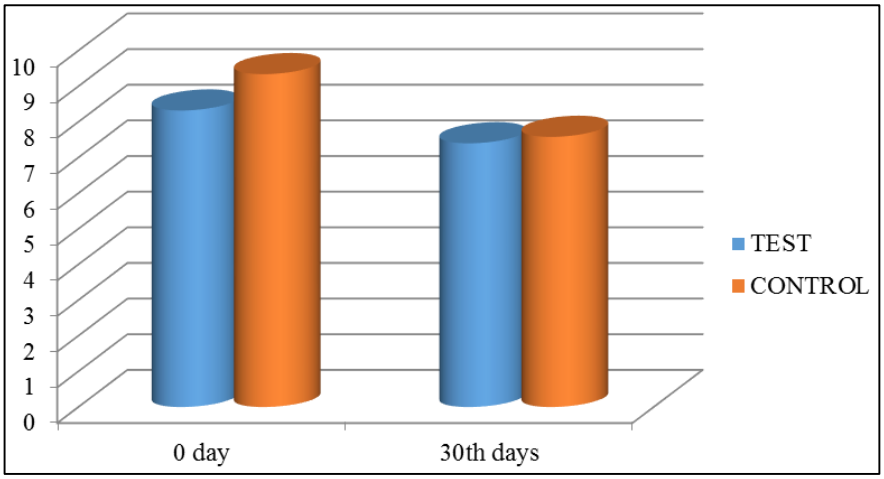

Fig 2: Effect of drugs on serum uric acid

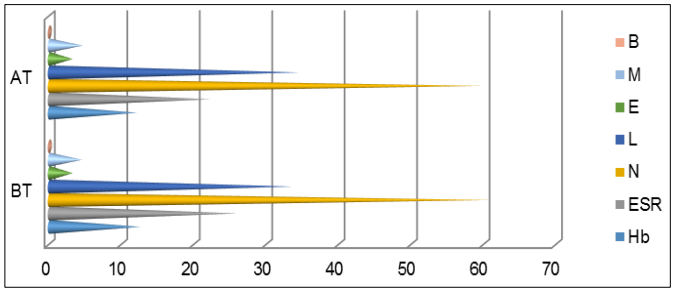

Fig 3: Effect of drugs on safety parameters (Hematological Parameters) Test Group

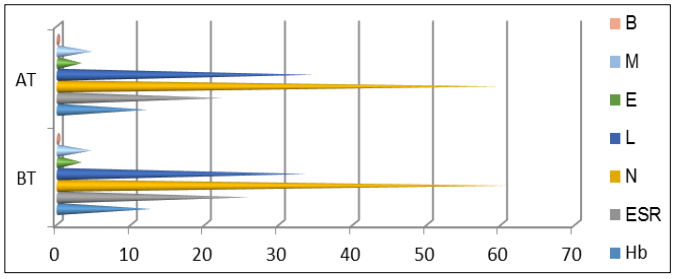

Fig 4: Control group BT = Before treatment, AT = After treatment, B = Basophil, M = Monocyte, E = Eosinophil, L = Lymphocyte, N = Neutrophil, ESR = Erythrocyte sedimentation rate, Hb = Hemoglobin

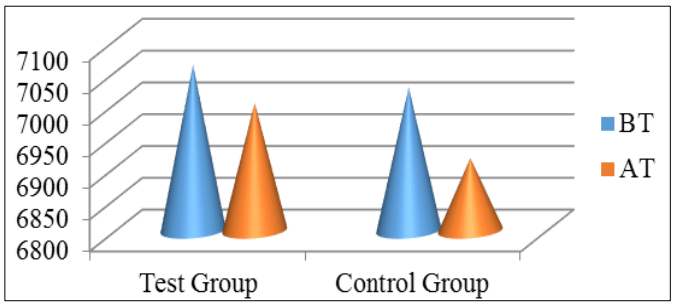

Fig 5: Effect of drugs on TLC BT = before treatment, AT = after treatment

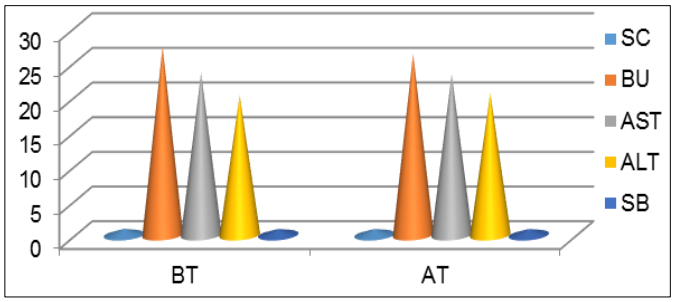

Fig 6: Effect of Drugs on Biochemical Parameters: Test Group

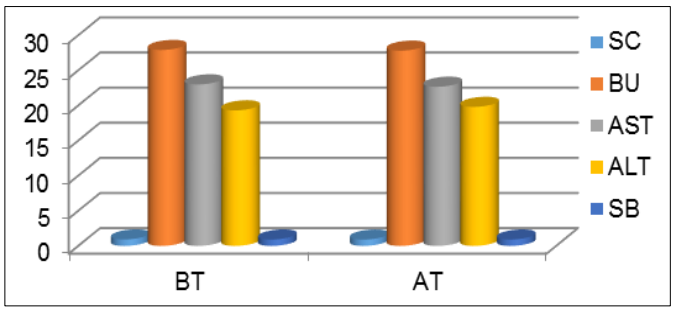

Fig 7: Control Group SC = Serum creatinine, BU = Blood urea, AST = Aspartate aminotransferase, ALT = Alanine aminotransferase, SB = Serum bilirubin

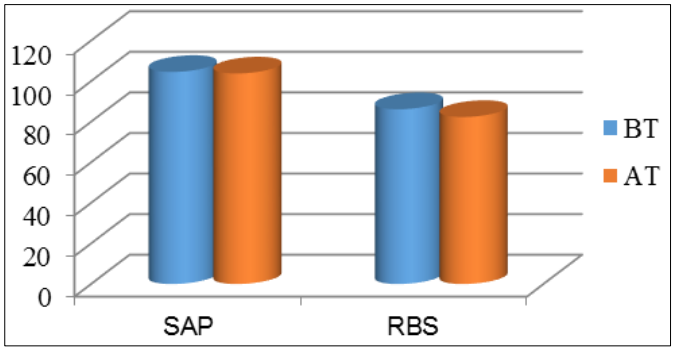

Fig 8: Test Group

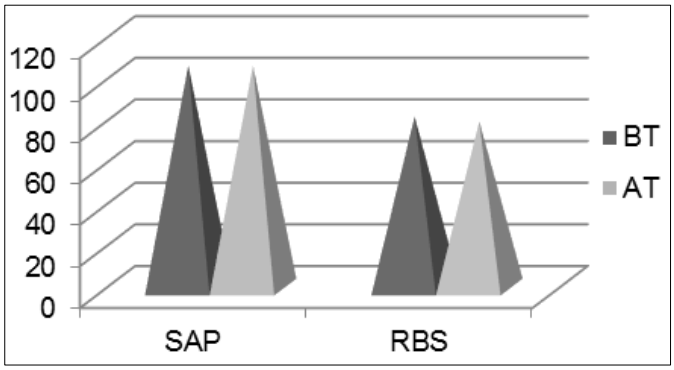

Fig 9: Control Group BT-=before treatment, AT=After treatment, SAP=Serum alkaline phosphatase, RBS=Random blood sugar

6. Acknowledgement

Authors are very grateful to Department of Moalijat, Faculty of Unani Medicine, Aligarh Muslim University, Aligarh-202002, for providing facilities to conduct the research. We are also thankful to the Ministry of AYUSH, New Delhi, for providing financial support and to the volunteers who participated in the study for their humble cooperation.

7. References

1. Syngle Ashit, Deodhar SD. Rheumatology Principles and Practice. Edn 1, Jaypee Brothers Medical Publisher (P) Ltd, New Dehli, 2010, 190-206.
2. Kopke A, Greeff OBW. Hyperuricaemia and Gout: Review. South African Family Practice. 2015; 57(1):6-12.
3. Schmitz Paul G, Martin Kewin J. Internal Medicine just the facts. Mc Graw Hill Medical Library of congress cataloging in Data, 2008, 733-738.
4. Ashtiyani, Changizi S, Golestanpour A, Shamsi M, Tabatabaei SM, Ramzani M. Rhazes' Prescription in Treatment of Gout. Iran Red Crescent Med J. 2012; 14(2):108-112.
5. Nuki George, Simkin Peter A. Review A Concise History of Gout & Hyperuricemia and Their Treatment. Arthritis Research & Therapy. 2006; 8(1):S1.
6. Goodman & Gilman's. The Pharmacological Basis of Therapeutics. Edn 12, McGraw Hill Medical Library of congress cataloging in Data, 2011, 994-1000.
7. March LM, Smith EUR, Díaz-Torné C, Perez-Ruiz F. Epidemiology of gout: An update. Best Practice & Research Clinical Rheumatology. 2010; 24:811-827.
8. Schlesinger Naomi, Mysler Eduardo. Canakinumab reduces the risk of acute gouty arthritis flares during initiation of allopurinol treatment: results of a double-blind, randomized study. Ann Rheum Dis. 2011; 70:1264-1271.

9. Longo Dan L, *et al*. Harrison's Principles of Internal Medicine, Edn 18, Mc Graw Hill Companies. 2012; 2:2837-2838, 3181-3185.
10. Schlesinger Naomi. Overview of the Management of Acute Gout and the Role of Adrenocorticotropic Hormone (Leading article). Drugs. 2008; 68(4):407-415.
11. Annemans L, Spaepen E, Gaskin M, Bonnemaire M, Malier V, Gilbert T, *et al*. Gout in the UK and Germany: prevalence, comorbidities and Management in general practice 2000-2005. Ann Rheum Dis. 2008; 67:960-966.
12. Goldman L, *et al*. Cecil Text Book of Medicine, Edn 23, Vol. II, Philadalphia: Saunders, 2007, 2069-2075, 3181-3185.
13. Nasimul H, Siddiqui MA, IQ Arshid, Sarferaz MD. An Overview of Niqris (Gout) and its interpretation with hyperuricemia. International Journal of Advanced Ayurveda, Yoga, Unani, Siddha and Homeopathy. 2013; 2:137-142.
14. Ledingham JGG, *et al*. Concise oxford textbook of medicine, Oxford university press, 1985, 970-75.
15. Sivera F. Multinational evidence-based recommendations for the diagnosis and management of gout: integrating systemic literature review and expert opinion of a broad panel of rheumatologists in the 3e initiative. Ann Rheum Dis. 2014; 73:328-335.
16. Khan Hakim Waliullah. (Original author Abu Mansoor-ul-Hasan Bin Nooh Qamri). Ghina Muna Ma Tarjuma-e-Minhajul Ilaj, 276-284.
17. Rhazi Abu Bakr Mohd Bin Zakariya. Kitabul Hawi (Urdu Translation), CCRUM Ministry of Health & Family Walfare New Dehli. 2004; 11:75-171.
18. Majusi Ali Bin Abbas. Kamilus Sana (Urdu Translation by Hakeem Ghulam Hussain Kintoori), Idara Kitabu sh Shifa, New Dehli. 2010; 2:507-514.
19. Baghdadi Ibn Hubal. Kitab Al-Mukhrat Fit Tibb (Urdu Translation by CCRUM), Ministry of Health & Family Welfare New Dehli. 2007; 4:79-95.
20. Qurshi Hakeem Mohd Hasan. Jam-ul-Hikmat, Part 1&2 combined, Idara Kitab-us-shifa, New Dehli. 2011; 1023:1025-1027.
21. Kabeeruddin Hakim Mohd. Tarjuma-e-Kabeer (Sharah-e-Asbab wa Alamat), part III, Hikmat Book Depot, Hyderabad, 1916, 189-191.
22. Arzani Hakim Mohd Akbar. Nuskha-e-Sahiha Tibb-e-Akbar (Urdu, Lucknow: Munshi Gulab Singh), 1893, 475.
23. Geelani Hakim Ghulam. Makhzan-ul-Jawahar, Mercantile Press Lahore, 1923, 898-900.
24. H Major Ralph Charles C. A History of Medicine, Edn 1, Thomas Illinos USA. 1954; 2:591-592.
25. Khan Hakeem Ghulam Jeelani. Makhzanul Ilaj (Jild I & II Combined), Idara Kitab-us-shifa, New Dehli, 2005, 698-702.
26. Khan Hakeem Mohd Azam. Akseer-e-Azam (Urdu Translation by Hakeem Kabeeruddin), Idara Kitab-us-shifa, New Dehli, 846-847.
27. Azeez Hakeem Abdul. Mufradat-e-Azeezi, Maktaba Sahitya Mandir Press Ltd, Luckhnow, 43-44, 56, 58, 80.
28. Ghani Hakeem Najmul. Khazainul Advia, Part I-IV, Idara Kitab us shifa, Daryaganj New Dehli, 308-312, 861-862, 1352-1354.
29. Arthritis Link. The History of Gout.www.about.com. 2001.
30. Tripathi KD. Essentials of Medical Pharmacology, Edn 7, (Reprint), JP Brothers Medical Publishers, 2014, 214-17.
31. Baghdadi Ibn Hubal. Kitab Al Mukhtarat Fit Tib (Urdu Translation by CCRUM), Ministry of Health and Family Welfare, New Dehli, 2007, 2:118, 209, 239-240.
32. Rhazi Abu Bakr Mohd Bin Zakariya. Kitabul al Mansoori (Urdu Translation), CCRUM Ministry of Health and Family Welfare, New Dehli, 1991, 136, 143, 145, 391-394.
33. Kirtikar KR, Basu BD. Indian Medicinal Plants, Edn 2, International Book Distributor, Dehradun. 1981; 4:2504.
34. Anonymous, The Unani Pharmacopoeia of Indian Plants, Part I, Vol. I, CCRUM Department of AYUSH Ministry of Health & Family Welfare, New Dehli, 2007, 64-65,32-33.
35. Looqa Qusta bin. Risala Fi Auja Al-Niqris (Urdu Translation by prof. Hkm. Syed Zillur Rehman), Ibn Sin Academy Dodhpur, Aligarh, 2007, 68-137.
36. Omole OB, Ogunbanjo GA. The evolution of gout (an old lifestyle disease). SA Fam Pract. 2009; 51(5):396-398.
37. Kirtikar KR, *et al*. Indian Medicinal Plants, Edn 2, International Book Distributor, Dehradun, 1981; 2:1020-1023, 1147.
38. Sharma PC, Velnu MB, Dennis TJ. Database on Medicinal Plants used in Ayurvedic (Vol I, III, V). CCRAS, 2002, 225-243.
39. Anonymous, Standard Unani Medical Terminology, Edn 1, CCRUM Department of AYUSH Ministry of Health and Family Welfare, New Dehli, 2012, 290,143.
40. Kabeeruddin Hakeem. Makhzanul Mufradat, Ejaz Publishing House, Daryaganj Dehli, 102-103, 363-364, 590-591.
41. Anonymous, the Unani Pharmacopoeia of Indian Plants, Part I, Vol. I, CCRUM Department of AYUSH Ministry of Health & Family Welfare, New Dehli, 2007, 64-65, 32-33.
42. Hakeem Abdul. Bustanul Mufradat Jadeed, Idara Kitab-us-shifa Kochla Chailan Daryaganj, New Dehli, 2002, 97, 193, 358-359, 502-503, 609.
43. Baitar Ziyauddin Abdullah Ibn. Aljamiul Mufradat Al Advia Wa Al Aghzia (Urdu Translation), Vol. III, CCRUM Ministry of Health and Family Welfare, New Dehli, 1999, 96-98, 170-175.
44. Tariq Naseer Ahmad. Khwas-ul-advia, Idara Kitab-us-Shifa Kocha Chelan Daryaganj, New Dehli, 105-107, 460, 759-761.
45. Nadkarni AK. Indian Materia Medica, Bombay Popular Prakashan. 1982; 1:278-279.