

# Comprehensive review on therapeutic strategies of gouty arthritis

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**Abstract:** Traditional medicines are practiced worldwide for treatment of gouty arthritis since ancient times. Herbs and plants always have been used in the treatment of different diseases such as gout. The present article deals with the therapeutic strategies and options for the cure of gouty arthritis. Bibliographic investigation was carried out by analyzing classical textbooks and peer reviewed papers, consulting worldwide accepted scientific databases. In this article a detailed introduction, classification, epidemiology, risk factors, symptoms, diagnosis and treatment of gout with reference to modern and Unani system of medicines have been discussed. It is also tried to provide a list of plants used in the treatment of gout along with their formulations used in Unani system of medicine. The herbs and formulations have been used in different systems of medicine particularly Unani system of medicines exhibit their powerful role in the management and cure of gout and arthritis. Most of herbs and plants have been chemically evaluated and some of them are in clinical trials. Their results are magnificent and considerable. However their mechanisms of actions are still on the way.

**Keywords:** Gouty arthritis, Unani medicine, treatment strategies, literature review

## INTRODUCTION

### *Gouty Arthritis (Naqras)*

Gout (*Naqras*) is known since age of antiquity and identified by the Egyptian in 2640BC. Hippocrates recognized the gout in the fifth century BC and described it as unwalkable disease. Hippocrates presented some clinical perception of gouty arthritis in aphorism. In Unani system of medicine, it is believed that an excessive intake of food containing high purine contents (*Baadi ghiza*) is the primary or essential cause of gouty arthritis (*Naqras*), which results in deposition of *Maddah-e-Naqris* (urates or tophi) in the articular and periarticular tissues. As early as the fourth century BC, Hippocrates wrote about gout (*Naqras*) as a disease of old men and a product of high profile life style (George & Peter, 2006). The eminent Greek physician Galen (BC 130-ca. 215) described tophi as the manifestation of longstanding gout (*Naqras*) and stated that a female body was to be affected less by gout (*Naqras*) (Konstantinos *et al*, 2011).

According to Al-Razi, gout (*Naqras*) occurs due to abnormal phlegm that reaches through blood to joints and involves them and they gradually get hardened and become stone like (Tabatabayee, 2009). An eminent Greek physician Diocles of Carystus (4th century BC) believed that gout (*Naqras*) was an inflammatory disease that occurs due to accumulation of bad humours in the feet joints. He further described that gout (*Naqras*) cold podagra (acute gout (*Naqras haad*)) that occurs in the first

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metatarsophalangeal joint is due to phlegmatic humours and warm padgra is due to choleric humours. The five aphorism on gout (*Naqras*) are described by Hippocrates, wherein it is ascertained that neither women before start of menses, nor the male before attaining puberty suffer from *Naqras*. In addition, in gouty arthritis, inflammation usually subsides within 40 days (Omole and Ogunbanjo, 2009). Hyperuricemia refers to an elevation in the serum uric acid concentration. This is sometimes associated with increased uric acid excretion called as uricosuria. At the physiological pH, uric acid is in a more soluble form as sodium urate. In severe hyperuricemia, uric acid is deposited in the joints; such deposits are known as tophi. Due to this reason, it causes inflammation in the joints resulting in a painful gouty arthritis (*Naqras*). Sodium urate and/or uric acid may also precipitate in kidneys and ureters that lead to renal damage and stone formation. Gout (*Naqras*) is often associated with eating of high protein diet and alcohol consumption. The prevalence of gout (*Naqras*) is about 3 per 1,000 persons, mostly affecting males (Anton *et al*, 1998). The common treatment of gout (*Naqras*) is by the use of anti-inflammatory agents and xanthine oxidase (XO) inhibitors to inhibit the synthesis of uric acid. Allopurinol is the most common xanthine oxidase inhibitor. However, its use is limited due to the side effects such as hypersensitivity. Therefore, alternatives treatment modes for gout (*Naqras*) are required. Some herbal medicines have been used traditionally by the Unani physicians as a uricosuric and depurative for treating gout (*Naqras*) (Rizwan, 1999; Saeed and Hameed, 1973).

### **Treatment of gout (Naqras)**

For the treatment of gout (*Naqras*) and gouty arthritis (*Naqras*), the Hippocratic said that acute pain in gout (*Naqras*) should be relieved first and then try to excrete out waste product (uric acid) through urine. He further said that treatment of gout (*Naqras*) takes long times but the disease will not lead to harm.

The treatment of gout (*Naqras*) with different drugs and their dosage form design are enumerated as under.

### **Classification of allopathic drugs used in gout (Naqras)**

#### **Based on mechanism of action**

- (i). Inhibit uric acid synthesis: Allopurinol
- (ii). Increase uric acid excretion: Probenecid, Sulphinpyrazone
- (iii). Inhibit neutrophil migration into joint: Colchicine
- (iv). Inhibit inflammation and pain: NSAIDs
- (V). Drugs increasing uric acid oxidation: Urate oxidase

#### **Bases on clinical use**

- (i). Drugs used in acute gout (*Naqras haad*): Colchicine, NSAIDs, Prednisolone
- (ii). Drugs used in chronic gout (*Naqras muzmin*): Allopurinol, Probenecid, Sulphinpyrazone

### **Asymptomatic hyperuricemia**

Asymptomatic hyperuricemia should not be treated, uric acid-lowering drugs need not be instituted until arthritis (*Waja-ul-mafasil*), renal calculi, or tophi become apparent.

### **Treatment of acute gouty arthritis (Naqras Haad)**

Indomethacin 100 mg followed by 25mg t.d.s or naproxen 750mg followed by 250mg t.d.s. is used. Hydrocortisone 100mg intramuscularly repeated as required may be given in resistant cases and may relieve pain almost instantaneously. Colchicine (0.5-1mg 2 hourly until pain is relieved, vomiting and diarrhea begin or a total of 8 mg) may be given if nonsteroidal anti-inflammatory drugs (NSAID) are contraindicated Colchicine is an alkaloid that is obtained from *Colchicum autumnale* (*Soranjan shirin*). This has been used as purgative in Unani system of medicine. Now it is prescribed to treat gout (*Naqras*). Colchicine inhibits neutrophil migration to urate deposited area, thereby decreasing phagocytosis of urates and inhibition of subsequent events inducing inflammation. It rapidly relieves pain and inflammation in acute gout (*Naqras*) but is ineffective in non-gouty arthritis (*Naqras*) (Roberts *et al*, 1987). Allopurinol may be started a fortnight after the acute attack has subsided but must be covered by continuation of non steroidal anti-inflammatory drug therapy or colchicine 0.5 mg b.d. until at least 1 month after hyperuricemia is corrected, because acute gout (*Naqras*) may otherwise be precipitated (George *et al*, 2010).

### **Synthetic adrenocorticotrophic hormone (ACTH)**

ACTH has been utilized in acute gouty arthritis (*Naqras Haad*). It is administered as an intramuscular or intravenous injection of 40-80 IU. Adrenocorticotrophic hormone causes glucocorticoid release from the adrenal cortex. If Adrenocorticotrophic hormone is discontinued, then relapse attacks, mild hypokalemia, glycemic control worsening, and fluid retention can take place. Other effects that make adrenocorticotrophic hormone a less attractive strategy as can be enumerated like cost, inconvenience of parenteral administration and dependence on the sensitivity of the adrenal cortex (Tahira *et al*, 2011).

### **Etoricoxib**

Nucoxia (Etoricoxib) is generally administered for the control of acute gouty arthritis (*Naqras*). Etoricoxib have given way to symptomatic relief in acute gouty arthritis (*Naqras Haad*) and osteoarthritis. Etoricoxib exhibits fewer side effects as compared to other NSAIDS. Therefore, it can be administered as a treatment alternate for patients given NSAID therapy, especially those at risk of upper gastrointestinal disturbance and uncontrolled hypertension. Etoricoxib should be prescribed at the lowest effective dose as well the duration of use should be minimized (Rubin *et al*, 2004).

### **Corticosteroids**

Oral corticosteroids (Cortef) are given to those patients who are unable to tolerate other anti-inflammatory drugs or colchicines. Corticosteroid should be avoided in diabetic patients. Intra-articular corticosteroid is recommended for single-joint involvement if infection does not prevail (Zhang *et al*, 2006).

### **Montelukast**

Montelukast (*Singuaire*) provides an efficient mode anti-inflammatory access in gouty arthritis (*Naqras*). Anti-leukotrienes have proved to be an effective therapy, either isolated or in combined with orthodox therapy of gouty arthritis (*Naqras*) (Loida *et al*, 2011).

### **Riloncept**

Riloncept (Arcalyst) is prescribed for treatment of chronic complicated gout (*Naqras*). It is prescribed when other treatment options fail to reduce pain in gout (*Naqras*). Interleukin 1 blockade suggests that riloncept is effective in patients with gout (*Naqras*) (Terkeltaub *et al*, 2009).

### **Treatment of chronic gouty arthritis (Naqras Muzmin)**

Treatment of chronic gout (*Naqras Muzmin*) is intended to minimize urate deposition in tissues and to reduce the frequency and severity of recurrences

### **Urate-Lowering Therapy (ULT)**

Urate lowering therapy is prescribed to maintain a serum urate level of <6mg/dL. This treatment option also

inhibits urate crystal formation and promotes crystal dissolution

Indications for urate lowering therapy (ULT) include:

- Chronic gouty arthritis (*Naqras*)
- 24 hours urinary urate excretion >1,000 mg
- Gout (*Naqras*) with chronic kidney disease (CrCl<60 mL/min)
- 3 or more gout (*Naqras*) flares per year
- Recurring renal stones
- Tophi
- Overproduction of uric acid

Urate lowering therapy is initiated and serum uric acid is measured after every 2-4 weeks and urate-lowering drugs titrated upward to doses that will achieve the targeted level (ie, <6.0 mg/dL). Non-adherence to urate lowering therapy (ULT) can result in recurring attacks and tophi development, therefore, individuals with hyperuricemia should be encouraged to continue urate-lowering therapy for life. Urate lowering agents are of three types such as xanthine oxidase inhibitors, uricosurics and urate oxidases (Zhang et al, 2006).

#### **Allopurinol**

It is purine compound with chemical similarity to hypoxanthine. Allopurinol decreases uric acid synthesis from hypoxanthine and xanthine by inhibiting the enzymes xanthine oxidase. This results in decrease of relatively insoluble urates in tissue with concomitant increase in soluble xanthine and hypoxanthine, which are readily excreted. Allopurinol is well absorbed from gut. It has a short half-life of 2 hours while that of alloxanthine is prolonged of 24 hours. Both are renally excreted. Allopurinol is used in chronic gout (*Naqras Muzmin*) and in prevention of acute exacerbations. In oral form, recommended dose of Allopurinol is 300-600 mg once daily. There is increased risk of acute gouty (*Naqras Haad*) attack during initial use of Allopurinol and manifestations exhibited are gastrointestinal disturbances, and skin rashes. Rarely, hepatic and renal failure may occur (Elasy et al, 1995). 6-mercaptopurine, allopurinol inhibits the metabolism and reduces dose requirement by 1/3, and hence shows toxicity. Azathioprine is biotransformed into 6-mercaptopurine and exhibits similar interaction. It increases toxicity of cyclophosphamide and oral anticoagulants by inhibiting their metabolism (Arellano and Sacristan, 1993).

#### **Uricosurics**

Uricosurics such as probenecid and sulfinpyrazone are involved in excretion of uric acid through the kidney. Uricosuric drugs inhibit tubular reabsorption of uric acid in the kidney. In the start of treatment, uricosuric drugs are given in low doses and dose is increased later on because large amounts of uric acid, passing through the kidneys, may precipitate and will form urate stones. Losartan 'a well known anti-hypertensive agent' is also involved in uric acid excretion. Losartan has uricosuric

like effect. Uricosuric drugs may aggravate pre-existing renal insufficiency. The uricosuric drugs are avoided in patients with kidney stones and kidney failure. Hence such types of patients should be treated with drugs that will function independently, not involving of kidney function (Yamamoto et al, 2002).

#### **Probenecid**

Probenecid inhibits renal tubular transport of organic acids, including uric acid and penicillin. However, in higher doses, probenecid inhibits active reabsorption of uric acid, the net effect promote a uricosuric action (Perkins & Jones, 1999). Probenecid is used in chronic gout (*Naqras Muzmin*) and hyperuricemia on administering probenecid Dosage: In gout (*Naqras*) 250-500mg orally twice daily; with penicillin, 500mg orally 6 hourly. These are mild gastrointestinal upsets and skin rashes. It may precipitate hemolytic anemia in the presence of glucose-6-phosphate dehydrogenase deficiency. Aspirin inhibits uricosuric effects of probenecid, whereas it increases toxicity of methotrexate and chloroquine through increased retention (Harris et al, 2000).

#### **Sulphinpyrazone**

It is chemically related to phenylbutazone and has a probenecid like uricosuric effect, with similar mechanism of action. As with probenecid, alkalization of urine and high fluid intake are required to avoid uric acid crystallization and formation of renal calculi. Clinical use is limited to chronic gout (*Naqras muzmin*) and hyperuricemia. Earlier use as cardio protective agent for prevention of reinfarction that inhibits platelet aggregation, due to this reason it has now been discontinued. Adverse effects are usually limited to gastrointestinal symptoms, and it is contraindicated in peptic ulcer (Freedman et al, 1995).

#### **Urate oxidase**

The drug can be used in lowering uric acid level by oxidizing uric acid. Probenecid is recommended as 10, 000 I.U. daily for 10 days. It causes significant reduction in serum uric acid level. It can be prescribed in severe gout (*Naqras*) with renal involvement and secondary hyperuricemia (Sundy et al, 2007).

#### **Pegloticase**

Pegloticase (*Krystexxa*) is a polyethylene glycol (PEG) conjugate of recombinant uricase. It causes the conversion of uric acid into allantoin, as a result, serum uric acid level is lowered. It is prescribed to patient with chronic gout (*Naqras muzmin*) when conventional treatment becomes ineffective. This is prescribed by intravenous (IV) infusion at doase of 8mg every two weeks. Pegloticase is useful for the treatment of chronic gout (*Naqras muzmin*) in adult patients that do not respond to conventional therapy (Sundy et al, 2011).

Plants used in Unani system of medicine for treatment of gout (Amit *et al*, 2010).

Botanical Name	Common Name	Family	Part used
<i>Abrus precatorius</i> L.	Crab's eye	Fabaceae	Leaves
<i>Abutilon indicum</i> L.	Country Mallow	Malvaceae	Root
<i>Aconitum violaceum</i> Jacq.	Monkshood	Ranunculaceae	Root
<i>Adenanthera pavonina</i> L.	Coral Wood	Leguminosae	Whole plant
<i>Aframomum melegueta</i> K.	Grains of paradise	Zingibraceae	Whole plant
<i>Agropyron repens</i> Beauv.	Couch grass	Gramineae	Rhizomes
<i>Ajuga bracteosa</i> Wall.	Khurbanti	Labiatae	Whole plant
<i>Alchornea cordifolia</i> Muell.	Christmas bush	Euphorbiaceae	Leaves
<i>Alhagi pseudalhagi</i> Medik	Camel Thorn	Papilionaceae	Whole plant
<i>Aquilaria agallocha</i> Roxb.	Aloe wood	Thymelaceae	Wood
<i>Armoracia lapathifolia</i> Gilib.	Horseradish	Cruciferae	Root
<i>Asparagus racemosus</i> willd.	Indian asparagus	Asparagaceae	Root
<i>Asteracantha longifolia</i> Nees	Bhikshu	Acanthaceae	Root
<i>Azadirachta indica</i>	Neem	Meliaceae	Leaves
<i>Barleria prionitis</i> L.	Barleria	Acanthaceae	Leaves
<i>Betula utilis</i> D. Don	Indian Paper tree	Betulaceae	Leaves
<i>Caesalpinia bonduc</i> (L.) Roxb.	Fever Nut	Caesalpiniaceae	Seeds
<i>Canella winterana</i> Gaertn.	Wild cinnamon	Canellaceae	Bark
<i>Capparis aphylla</i> Roth.	Caper Berry	Capparidaceae	Root
<i>Capparis decidua</i> (Forsk) Edgew	Amargna	Capparidaceae	Root
<i>Capparis spinosa</i> L.	Common Caper- bush	Apparidaceae	Whole plant
<i>Cassia fistula</i> L.	Cassia stick	Caesalpiniaceae	Pulp
<i>Cassia senna</i> L.	Indian Senna	Leguminosae	Leaves & pods
<i>Celastrus paniculatus</i> Willd.	Staff tree	Celastraceae	Seeds
<i>Chrysanthemum indicum</i> L.	Chrysanthemum	Asteraceae	Twig
<i>horium intybus</i> Linn.	Chicory	Compositae	Whole plant
<i>Cinnamomum cassia</i> Linn.	Cassia Bark	Lauraceae	Twig
<i>Clematis recta</i> Roxb.	Muurvaa	Ranunculaceae	Whole plant
<i>Cocculus hirsutus</i> (Linn.) Diels.	Broom-Creeper	Menispermaceae	Root
<i>Colchicum autumnale</i> L.	Naked lady Lily	Liliaceae	Seeds
<i>Costus speciosus</i> (Koenig) Sm.	Canereed	Canereed	Whole plant
<i>Croton menthodor</i> Benth	Chala	Euphorbiaceae	Seeds, leaves
<i>Cymbopogonjwarancusa</i> Schult	Bhuutikaa	Poaceae	Whole plant
<i>Cymbopogon proximus</i> Stapf.	Lemon grass	Poaceae	Leaves
<i>Datura stramonium</i> L.	Thorn apple	Solanaceae	Leaves
<i>Daucus carota</i> Linn.	Carrot	Umbelliferae	Root
<i>Delphinium denudatum</i> Wall.	Larkspur	Ranunculaceae	Root
<i>Dodonaea viscosa</i> (L.) Jacq.	Hopseed	Sapindaceae	Whole plant
<i>Ecbolium linneanum</i> Kurz	Blue Fox Tail	Acanthaceae	Whole plant
<i>Euphorbia antiquorum</i> L.	Triangular Spurge	Euphorbiaceae	Stem
<i>Eutrochium purpureum</i> L.	Joe Pye weed	Asteraceae	Root & leaves
<i>Exacum pedunculatum</i> L.	Ava-chiraayataa	Gentianaceae	Whole plant
<i>Fagus sylvatica</i> Linn.	European Beech	Fagaceae	Seeds
<i>Flacourtia indica</i> (Burm.f.). Merr.	Indian plum	Flacourtiaceae	Bark
<i>Flacourtia sepiaria</i> Roxb.	Vikankata	Flacourtiaceae	Bark
<i>Galium verum</i> Linn.	Lady's Bedstraw	Rubiaceae	Whole plant
<i>Gloriosa superba</i> Linn.	Glory Lily	Liliaceae	Seeds, tubers
<i>Gnaphalium luteo-album</i> Linn.	Jersey Cudweed	Asteraceae	Leaves
<i>Guaiacum sanctum</i> L.	Hollywood	Zygophyllaceae	Resin
<i>Gynocardia odorata</i> R.Br.	Chaalmograa	Flacourtiaceae	Seeds
<i>Helianthus annuus</i> Linn.	Sun?ower	Compositae	Tubers

Continued...

Table: Continue

<i>Heliotropium curassavicum</i> L.	Wild heliotrope	Boraginaceae	Whole plant
<i>Hollarhena antidysenterica</i> Wall	Kurchi	Apocynaceae	Bark
<i>Hyptis verticillata</i> Jack.	Wild mint	Labiatae	Rhizomes
<i>Iberis amara</i> Linn. Rocket	Candytut	Cruciferae	Whole plant
<i>Ilex paraguariensis</i> St.-Hil	Mate Tea	Aquifoliaceae	Whole plant
<i>Indigofera tinctoria</i> Linn.	Indigo	Fabaceae	Whole plant
<i>Jateorhiza micrantha</i> Hook.f	Flat hand of monkey	Menispermaceae	Leaves
<i>Kalmia</i> sp.	Laurel de la montana	Ericaceae	Leaves
<i>Lanneacoromandelica</i> (Houtt.)Merrill.	Jingini	Anacardiaceae	Bark
<i>Larix laricina</i> W. Wight	Black larch	Pinaceae	Whole plant
<i>Launaea sarmentosa</i> Wild.	Littoral Spine grass	Asteraceae	Whole plant
<i>Ledum palustre</i> L.	Rosa Marina	Ericaceae	Fresh plant
<i>Lepidium sativum</i> Linn.	Garden Cress	Curciferace	Seeds
<i>Linum usitatissimum</i> L.	Linseed	Liliaceae	Seeds
<i>Liriodendron tulipifera</i> L.	Tulip tree	Magnoliaceae	Wood
<i>Lycopus europaeus</i> L.	Gypsywort	Lamiatae	Leaves
<i>Mesua ferrea</i> Linn.	Iron-wood	Guttiferae	Stamens
<i>Michelia champaca</i> Linn.	Champak	Magnoliaceae	Flowers
<i>Miliusa velutina</i> Hook. f. &homs.	Rshiyaproktaa	Annonaceae	Bark
<i>Mollugo cerviana</i> Ser.	Threadstem carpetweed	Aizoaceae	Root
<i>Momordica charantia</i> Linn.	Bitter gourd	Cucurbitaceae	Fruits, leaves
<i>Morinda citrifolia</i> Linn.	Indian Mulberry	Rubiaceae	Root
<i>Moringa oleifera</i> Lam.	Moringa	Moringaceae	Seeds
<i>Nicotiana tabacum</i> Linn.	Tobacco	Solanaceae	Leaves
<i>Orthosiphon grandiflorus</i> Boldingh.	Kidney Tea Plant	Labiatae	Leaves
<i>Papaver rhoeas</i> L.	Corn poppy	Papveraceae	Leaf, flowers
<i>Petroselinum crispum</i> L. Mill.	Parsley	Apiaceae	Seeds, Leaves
<i>Physalis alkekengi</i> Linn.	Strawberry Tomato	Solanaceae	Fruits
<i>Physalis minima</i> Linn.	Sun-berry	Solanaceae	Fruits
<i>Physalis peruviana</i> L.	Cape Gooseberry	Solanaceae	Whole plant
<i>Polygonum cuspidatum</i> Sieb	Japanese knotweed	Polygonaceae	Rhizome
<i>Premna integrifolia</i> Linn.	Headache tree	Verbenaceae	Whole plant
<i>Plantago ovata</i> Forsk.	Aspagol	Plantaginaceae	Seeds
<i>Ranunculus arvensis</i> Linn.	Corn Buttercup	Ranunculaceae	Whole plant
<i>Ranunculus muricatus</i> Linn.	Water Crowfoot	Ranunculaceae	Whole plant
<i>Rhododendron</i> sp.	Rosa de Siberia	Ericaceae	Leaves
<i>Ruscus aculeatus</i> L.	Butcher's Broom	Liliaceae	Rhizome
<i>Salix alba</i> Linn.	White Willow	Salicaceae	Whole plant
<i>Sapindus laurifolius</i> Vahl .	Soapnut tree	Sapindaceae	Root
<i>Sapindus trifoliatus</i> L.	Soapnut Shells	Sapindaceae	Root
<i>Sassafras albidum</i> (Nutt.) Nees	Ague tree	Lauraceae	Root
<i>Saussurea lappa</i> (Decne) Sch. Bip.	Kuth	Compositae	Root
<i>Schinus terebinthifolius</i> Raddi.	Brazilian Pepper	Goodeniaceae	Whole plant
<i>Scoparia dulcis</i> L.	Broomweed	Scrophulariaceae	Whole plant
<i>Semecarpus anacardium</i> Linn. f.	Marking-Nut	Anacardiaceae	Whole plant
<i>Solanum nigrum</i> Linn.	Black Nightshade	Solanaceae	Leaves
<i>Spilanthes oleracea</i> Murr.	Brazilian Cress	Compositae	Flowers
<i>Tanacetum vulgare</i> Linn.	Tansy	Compositae	Whole plant
<i>Thalictrum foliolosum</i> DC.	Pitarangaa	Ranunculaceae	Whole plant
<i>Trema orientalis</i> L.	Pigeon wood	Cannabaceae	Leaves
<i>Trewia nudiflora</i> Linn.	False White Teak	Euphorbiaceae	Root

Continued...

**Table:** Continue

<i>Tribulus terrestris</i> L.	Gokharu	Zygophyllaceae	Seeds
<i>Trigonella foenum-graecum</i> L.	Menthi	Fabaceae	Seeds
<i>Urtica dioica</i> L.	Stinging Nettle	Urticaceae	Whole plant
<i>Vateria indica</i> Linn.	White Damar	Dipterocarpaceae	Resin
<i>Verbascum thapsus</i> Linn.	Gadar tambakoo	Scrophulariaceae	Leaves
<i>Vitis vinifera</i> Linn.	Wine Grape	Vitaceae	Fruits
<i>Withania somnifera</i> Linn.	Ashwagandha	Solanaceae	Root & stem
<i>Ziziphus jujuba</i> (Lam.) Gaertn.	Indian Jujube	Rhamnaceae	Root
<i>Zygophyllum coccineum</i> L.	Zygophyllum	Zygophyllaceae	Fruit & seeds

### Fenofibrate

Fenofibrate (Fenoglide) has been cited in the literature to treat hyperlipidemia. The drug decreases serum urate level and long-term administration of fenofibrate exerts substantial and sustained decrease in serum urate. This results in the decrease in acute gout (*Naqras haad*) attacks. Many cases have been reported to be relieved attacks with the use of fenofibrate (Sarawate *et al*, 2006).

### Unani management

Unani medicine has rationale and scientific principles, where in the plant or its parts or its aqueous or alcoholic fractions as such are utilized to formulate dosage form design.

Al-Razi stated that management of gout (*Naqras*) can be achieved if these ten procedures are followed:

1. Taking preventive measures to avoid recurrence of gouty attacks
2. Application of water to the feet types and drinks
3. Bloodletting
4. Stimulations of emesis
5. Steam baths
6. Compliance with fluid and dietary regimens regarding the emphasis on certain food
7. Treatment with salves and poultices
8. Administration of laxatives
9. Abstinence from restricted diet
10. Prompt management of incipient gout (*Naqras*) using counter-acting drugs and Analgesics (Ashtiyani *et al*, 2012).

### Precautions and dietary recommendation

Al-Razi stated that "Gouty patients should be restricted camels meat, beef, namaksud (salted jerked meat) (Ashtiyani *et al.*, 2012).

Al-Razi stated that Cereal should not be consumed such as beans and gram peas. He further stated that beans and gram peas should be avoided in patients suffering from gout (*Naqras*) having biliary blood and rice and chickpeas are restricted in patients with with phlegmatic blood. Furthermore, eggs can be eaten, if they are soft boiled. Al-Razi stated that dried fruits such as almond can be eaten. According to Al-Razi, almond is the most recommendable

among the dried fruits. Patients suffering from gout (*Naqras*) can eat fruit that have moderate moderate sweetness, such as fully ripened grapes, figs, apples, pomegranate, quince and pears. Vegetables that are allowed for patients suffering from gouty arthritis include lettuce, endives, dodder and *Apium graveolens* (*Tukhm-e-karafs*) for they have least harm to gouty patients (Ashtiyani *et al*, 2012). The purine contents in food and beverages also play a part in the initiation of gout (*Naqras*), therefore, food that contain high level of purine content should be avoided.

### Unani formulations prescribed in gout (Naqras)

Different approaches on prescription on treatment of gout (*Naqras*) in a different dosage form of Unani medicine has been cited in Haziq by Hakim Ajmal Khan and herbal drugs and herbalist in Pakistan, which are as under;

#### Formulation No. 1

##### During initial stage

Following combination of formulations should be given for a few days. *Majun Suranjan* 7g bid along with the following formulation based on single drug therapy: *Tribulus terrestris* (*Kharkhask*) 3g, *Cucumis sativus* (*Kheera*) 3g, Both of the drugs are grinded and are administered with 3 spoonfuls of *Sharbat-e-buzoori*. For local application: Oil of *Lawsonia inermis* (*Henna*, *Mehndi*) is applied on the site of pain (Masih and Ajmal, 1970).

#### Formulation No. 2

*Colchicum autumnale* (*Suranjan shirin*) 5g, *Viola odorata* (*Gul-e-banafsha*) 7g, *Swertia chirata* (*Chiretta*) 7g, *Zizyphus jujubae* (*Unnab*) 5g, *Solanum nigrum* (*Inababus salab khushk*) 5g, *Foeniculum vulgare* (*Baikh Badyan*) 5g, *Fumaria indica* (*Shahtra*) 5g, *Polygonum vulgare* (*Bisfaij*) 7g, *Fumaria indica* (*Shahtra*) 7g, *Foeniculum vulgare* Mill (*Badyan*) 7g, all these drugs are placed in hot water. Then gulqand 4g or *Alhaji maurorum Medica* (*Taranjibin*) 4g is added and administered to the patient. At tenth day: The formulation mentioned below is prepared to administer the patient. *Rosa damacenna* (*Gul surkh*) 7g, *Cassia senna* (*Sana maki*) 7g, Both drugs are added in this prescription and is percolated in water. At

morning: Maghz Floos 5g, *Tamarix indica* gum (*Taranjabeen*) 4g, Gulqand 4g, Red sugar 4g, all these drugs are added in syrup simplex (concentrated sugar solution) Maghz floos and is administered. At night: *Hab e Ayaraj* 9g is used as usual or *Hab e Suranjan* 5 tablets is administered. *Majoon Ushba* 7g or *Majoon Azaraqi* 3 g or *Majun Suranjan shirin* 7g with *Arq e Ushba* (*Smilax Medica*) 10 ml and misri 2g is administered. *Habb e Gul Akh* 2 tables or *Habb e Suranjan* 7g or *Calotropis procera* tablets (*Habb-e-Azaraqi*) bid is administered with *Arq-e-Mako* 12ml (Masih and Ajmal, 1970).

#### Formulation No. 3

In acute pain: *Lowsonia inermis* leaves (*Berg-e-Hina khushk*) and *Sabon desi* (*Soap*) 1g, both the ingredients are heated in vinegar (*Sirka*) upto this extent that the mixture seems to be thick and viscous like ointment. *Strychnos nuxvomica* L. oil (*Roghan kuchla*) or *Calotropis gigantea* L. oil (*Roghan gul akh*) and *Saussurea lappa* oil (*Roghan qast*) or *Roghan surkh* any one of them is messaged at joint pain. At night: *Sabar sqootri* 1g, *Convolvulus scammonia* (*Sqmoonia mushvi*) 1g, *Operculina turpith* (*Turbid sufaid*) 1gm, *Colchicum autumnale* (*Suranjan shirin*) 1g, *Polyporus officinalis* (*Ghariqoon*) 1 gm, *Cassia senna* (*Sana maki*) 1g, *Zingiber officinale* (*Zinjbeel*) 1g, five tablets should be administered at night (Masih and Ajmal, 1970).

#### Formulation No. 4

*Fumaria indica* concotive (*Shahtra*) 7g, *Swertia chirata* (*Chirata*) 7g, *Tephrosia purpurea* (*Sarphuka*) 7g, *Sphaeranthus indicus* (*Mundi*) 7g, *Ziziphus jujuba* (*Unab*) 5 fruits, *Terminalia bellerica* (*Halila siya*) 7g, *Smilax regelli* (*Ushba maghrabi*) 7g. These ingredients are percolated in water at night and in morning it is administered with syrup *Bazoori*. As laxative: *Arq Matbookh haft roza* as laxative should be administered or 1 125mg kafoor (*Camphor*) after mixing in *Dawa e siyah mus-hal* 250 mg is administered with milk. This is used as a laxative so that waste material is eliminated. As massage

*Arq-e-Ajeeb* 5 drops are mixed in *roghan surkh* 1g or *orrogan qast* (*Saussurea lappa*) 1g and is massaged which help to relieve pain. As strengthening agent: At morning: After this, *Dawa ul Misk Motadil Jawahir* wali 5g or *Majun Chobchini banuskha khas* 5g or *Khamira Abresham Hakim Arshad* wala 5g is given for few days to strengthen the body defense system and to build up stamina. After meal: *Habb-e-Asab* 1 tablet or *Habb-e-Khas* 1 tablet is administered. At night *Jauhar-e-Munnaqa* 30mg is mixed in deseeded *Maveez Munnaqa* (*Raisin*). *Maveez Munnaqa* (*Raisin*) is administered without chewing (Masih and Ajmal, 1970)..

#### As Paste

*Euphorbia caducifolia* (*Ferfeon*) 2.5g, *Castoreum* (*Jund bedaster*) 1g, *Colchicum luteum* (*Suranjan talkh*) 6g,

*Ferula galbaniflua* secretion (*Jaosheer*) 3g. All ingredients are converted into powder in rose aqua and is pasted at joint. *Opium seeds* (*Tukhm e Khashkhas*) 1 g in goat milk 10ml is pasted at joint (Masih and Ajmal, 1970).

#### Formulation No. 5

Morning: *Viola odorata* (*Gul banafsha*) 4g, *Vitis vinifera* (*Maveez munaqqa*) 9 grains, *Cichroium intybus* (*Baikh kasni*) 5g, *Foeniculum vulgare* (*Badyan*) 3g, *Borago officinalis* (*Gao zaban*) 3g, *Lavendula stachados* (*Ustukhudus*) 3g, *Glycyrrhiza glabra* (*Aslus sus muqassar*) 4g. After noon: *Aujai* 2, Night: *Majun e Chobchini* 6g (Usmanghani et al, 1986).

#### Formulation No. 6

Morning and night: *Dawa ul Misk Motadil Sada* 6 g is administered with 1 gram of *Suranjan shirin* partially crushed and 1 g of *Chobchini* partially crushed 1g along with boiled water. Afternoon: *Tab. Aujai* 2 with fresh water (Usmanghani et al, 1986).

#### Formulation No. 7

Morning: *Khamira Hamdard* 6 g with *Sharbat-e-Bazoori* 12 ml dissolved in water, Afternoon: *Aujai* 1, Night: *Habb-e-Suranjan* 1, *Habb-e-Asgand* 1, *Habb-e-Kasirul Hayatain* 2 (Usmanghani et al, 1986).

#### Formulation No. 8

Morning: *Colchicum autumnale* (*Suranjan shirin*) 3g, *Smilax chinensis* (*Chobchini*) 3g, *Withania somnifera* (*Asgand*) 3g, *Cucumis sativus* (*Tukhm-e-khyarain*) 5g, *Glyccrhiza glabra* (*Badyan*), *Foeniculum vulgar* (*Aslus sus*) 5g, Afternoon: *Aujai* 2, Night: *Majun-e-Ushba* 5g, The above medication is very useful in headache, arthritis (*Waja-ul-mafasil*) or gouty arthritis (*Naqras*). In the beginning it should be dispensed twice daily (bid). From the second week: *Qurs e Aujai* 2 daily in the evening. From the third week one *Qurs-e-Mulaiyin*. In case of loose motion, the dose of *qurs e mulaiyin* is to be reduced to a half (Usmanghani et al, 1986)..

## CONCLUSION

The herbs and formulations have been used in different systems of medicine particularly Unani system of medicines exhibit their powerful role in the management and cure of gout and arthritis. Most of herbs and plants have been chemically evaluated and some of them are in clinical trials. Their results are magnificent and considerable. However their mechanisms of actions are still on the way.

## REFERENCES

- Amit A, Parveen B, Vikas G, Ranjit S and Amrendra K (2010). Pharmacological potential of medicinal plant used in treatment of gout. *Drug Inven. Tod.*, 2: 433-435.

- Anton F, Garcia J and Ramos T (1998). Sex differences in uric acid metabolism in adults: Evidence for a lack of influence of estradiol-17 on the renal handling of urate metabolism. *J. Metab.*, **35**: 343-348.
- Arellano F and Sacristan JA (1993). Allopurinol hypersensitivity syndrome: A review. *The Ann. Pharmacother.*, **27**: 337-343.
- Ashtiyani C, Golestanpour A, Shamsi M, Tabatabaei M and Rhazes M (2012). Prescriptions in treatment of Gout. *Iran. Red. Cres. Med. J.*, **4**: 108-112.
- Elasty T, Kaminsky D, Tracy M and Mehler P (1995). Allopurinol hypersensitivity syndrome revisited. *The West. J. Med.*, **162**: 360-361.
- Freedman D, Willianson D, Gunter E and Byers T (1995). Relation of serum uric, acid to mortality and ischemic heart disease. The NHANES 1 epidemiologic follow-up study. *Am. J. Epidemiol.*, **141**: 637-644.
- George N and Peter A (2006). A concise history of gout (Naqras) and hyperuricemia and their treatment. *Arthritis Res. Ther.*, **8**: 1-5.
- George T, James M and Hugues R (2010). Gout, allopurinol Use and heart failure outcomes. *Arch. Intern. Med.*, **170**: 1358-1364.
- Harris M, Bryant L, Danaher P and Alloway J (2000). Effect of low dose daily aspirin on serum urate levels and urinary excretion in patients receiving probenecid for gouty arthritis. *J. Rheumatol.*, **27**: 2873-2876.
- Konstantinos C, Marianna K and George A (2011). Gout (Naqras) in the writings on eminent ancient greek and byzantine physicians. *Acta Med. Hist. Adriat.*, **9**: 83-88.
- Loida P, Marjorie A, Gustavo B and Stuart A (2011). The effect of montelukast in a model of gouty arthritis induced by sodium monourate crystals. *Invest Clin.*, **52**: 15-22.
- Masih M and Ajmal K (1970). Gout. *Haziq sheikh Muhammad Bashir and Sons, Urdu Bazar Lahore*, **1**: 374-376.
- Omole O and Ogunbanjo G (2009). The evolution of gout (Naqras) (an old lifestyle disease). *South Afric. Fam. Prac.*, **51**: 396-398.
- Perkins P and Jones A (1999). Gout. *Ann Rheum. Dis.*, **58**: 611-616.
- Rizwan HA (1999). Naqras (gout). *Sharah Asbab, Maktaba Darul Taleefat. Khuda Dad. Colony*, **3**: 220-240.
- Roberts WN, Liang MH and Stein SH (1987). Colchicine in acute gout reassessment of risks and benefits. *J. Am. Med. Assoc.*, **257**: 1920-1922.
- Rubin B, Burton R and Navarra S (2004). Efficacy and safety profile of treatment with etoricoxib 120mg once daily compared with indomethacin 50mg three times daily in acute gout: A randomized controlled trial. *Arthritis Rheum*, **50**: 598-606.
- Saeed H and Hameed A (1973). Acute and chronic gout. *Tajarbat e Tabib Hamdard Academy, Karachi*. **1**: 458-471.
- Sarawate C, Patel P, Schumacher H, Yang W, Brewer K and Bakst A (2006). Serum urate levels and gout flares: analysis from managed care data. *J. Clin. Rheumatol.*, **12**: 61-65.
- Sundy J, Baraf H, Yood R, Edwards N, Gutierrez S, Treadwell E, Horowitz Z, Huang W, Maroli A, Waltrip R, Hamburger S and Becker M (2011). Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment. *J. Am. Med. Assoc.*, **306**: 711-720.
- Sundy J, Ganson N, Kelly S, Scarlett E, Rehrig C, Huang W and Hershfield M (2007). Pharmacokinetics and pharmacodynamics of intravenous PEGylated recombinant mammalian urate oxidase in patients with refractory gout. *Arthritis Rheum.*, **56**: 1021-1028.
- Tabatabayee S (2009). Gout. *Abreviation of Al-Hawi. Publication of Mashhad University of Medical Sciences*, **1**: 87-188.
- Tahira S, Ghazala S, Akram M and Laila S (2011). Management Of Acute Gout: A review Article. *Inter. J. Pain. Sym. Cont. Pall. Car.*, **8**: 80-82.
- Terkeltaub R, Sundy J, Schumacher H, Murphy E, Biedermann S, Wu R and Mellis S (2009). The interleukin 1 inhibitor rilonacept in treatment of chronic gouty arthritis: Results of a placebocontrolled, monosequence crossover, nonrandomised, single-blind pilot study. *Ann. Rheum. Dis.*, **68**: 1613-1617.
- Usmanghani K, Gisho H and Miki W (1986). Treatment of Gout. *Herb drugs herb. Pak.*, **28**: 74-75.
- Yamamoto T, Moriwaki Y and Takahashi S (2002). A simple method of selecting gout patients for treatment with uricosuric agents, using spot urine and blood samples. *J. Rheumatol.*, **29**: 1937-1941.
- Zhang W, Doherty M and Bardin T (2006). EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ESCISIT). *Ann. Rheum. Dis.*, **65**: 1312-1324.