Comprehensive review on therapeutic strategies of gouty arthritis

Muhammad Akram[1], Khan Usmanghani[2], Iqbal Ahmed[3], Iqbal Azhar[4] and Abdul Hamid[5]

[1]Department of Eastern Medicine and Surgery, Faculty of Medical and Health Sciences, The University of Poonch, Rawalakot, Azad Jammu & Kashmir, Pakistan
[2]Faculty of Eastern Medicine and Surgery, Hamdard University Karachi Pakistan
[3]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Baqai Medical University Karachi, Pakistan
[4]Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, Karachi
[5]Department of Horticulture, Faculty of Agriculture, The University of Poonch, Rawalakot, Azad Jammu & Kashmir, Pakistan

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 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).

**Corresponding author:* e-mail: makram_0451@hotmail.com

***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 adrenocorticotropic 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. Adrenocorticotropic hormone causes glucocorticoid release from the adrenal cortex. If Adrenocorticotropic hormone is discontinued, then relapse attacks, mild hypokalemia, glycemic control worsening, and fluid retention can take place. Other effects that make adrenocorticotropic 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 (*Singuair*) 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).

Rilonacept

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

Continued…

Table: Continue

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

Continued…

Table: Continue

Tribulus terrestris L.	Gokharu	Zygophyllaceae	Seeds
Trigonella foenum-graecum L.	Menthi	Fabaceae	Seeds
Urtica dioica L.	Stinging Nettle	Urticaceae	Whole plant
Vateria indica Linn.	White Damar	Dipterocarpaceae	Resin
Verbascum thapsus Linn.	Gadar tambakoo	Scrophulariaceae	Leaves
Vitis vinifera Linn.	Wine Grape	Vitaceae	Fruits
Withania somnifera Linn.	Ashwagandha	Solanaceae	Root & stem
Ziziphus jujuba (Lam.) Gaertn.	Indian Jujube	Rhamnaceae	Root
Zygophyllum coccineum 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 bens 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*roghan qast* (*Saussurea lappa*) 1g and is massaged which help to releive pain. As strenghtening 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 strenghten the body defense system and to build up stamina. After meal: *Habb-e-Asab* 1 tablet or *Habb-e-Khas* 1 tablet is adminstered. 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. Pharmacothe.,* **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.

Elasy 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 epidemiolologic 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 byzantuine 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. *Abrevation 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.