



Review Article

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ETIOPATHOGENESIS AND MANAGEMENT OF WAJA'AL-MAFĀSIL (RHEUMATOID ARTHRITIS): AN EVIDENCE-BASED COMPREHENSIVE REVIEW

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by symmetrical inflammatory polyarthritis involving small joints of the hand and feet. It has a global prevalence of 0.8 to 1% in Europe and the Indian subcontinent. Rheumatoid arthritis (Waja'al-Mafāsil) had been broadly described and managed by the Unani scholars since antiquity. Many pharmacological and non-pharmacological treatment methods are available in the classical Unani literature. The treatment differs for different varieties of morbid humour involved in disease pathogenesis. Treatment aims to reduce morbidity and prevent disability, subsequently improving the quality of life. This review article mainly highlights the management of rheumatoid arthritis mentioned in classical Unani literature and supportive scientific evidence of various preclinical and clinical studies suggesting the potential of Unani medicine. This review article aims to explore the concept of rheumatoid arthritis in the Unani system of medicine to provide a better understanding of disease and its management through the holistic policy of Unani medicine. This review may conclude that Unani treatment can form an alternative source to manage RA.

Keywords: Waja'al-Mafāsil, Rheumatoid arthritis, Etiopathogenesis, Unani management, clinical Trial, polyherbal Unani formulations

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune, systemic inflammatory disorder with characteristic deforming symmetrical polyarthritis of varying extent and severity, associated with synovitis of joint and tendon sheaths, articular cartilage degradation, erosion of juxta-articular bone, osteopenia, positive IgM rheumatoid factor, and anticitrullinated protein antibodies (ACPAs) in most of the patients. In some patients, systemic and extra-articular features manifest during the disease and rarely before articular involvement.^{1,2} RA is a heterogeneous disease because of its variable severity, unpredictable disease course, and variable response to treatment.³ This disease is a major global public health challenge, although the burden of RA fluctuates geographically. The overall prevalence and incidence rates are increasing globally. According to GBD 2017, about 20 million prevalent cases, 1.2 million incident cases, and 3.4 million DALYs. The highest incidence and prevalence of RA have been found in South Asia, including Bangladesh, India, Nepal, Bhutan, and Pakistan.⁴ It causes premature death and lowers the quality of life in the industrialized and developing world.⁵ The originating cause of RA is not known. However, the aetiology of the disease is multifactorial and associated with genetic, environmental, and host factors.^{1,2} It is mainly related to genetic susceptibility, epigenetic modifications, smoking, and exposure to infectious agents such as viruses, bacteria, and gut and oral microbiome.⁶

In the era of advanced medical care and extensive research, no permanent cure is available for RA. The primary treatment goals are to achieve the lowest possible disease activity, remission and recovery, minimize joint injury, improve the physical function

and quality of life.⁷ The conventional treatment options like non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, Disease-modifying anti-rheumatic drugs (DMARDs), and biologics are effective but associated with several adverse effects. NSAIDs cause gastric irritation; corticosteroids cause impaired wound healing, osteoporosis, and peptic ulcers on long-term use. DMARDs are associated with side effects like liver and kidney dysfunctions, whereas biologics suppress the immune system, which leads to bacterial and fungal infections.^{7,8} RA itself increases the risk of infection, also DMARDs and biologic therapies suppress the immune system through various targets, which further adds to the risk. Tumour necrosis factor (TNF) blockers also increase the risk of severe and systemic fungal infections. In addition, it increases the incidence of lymphoma and reactivates latent tuberculosis.⁹ Unani system of medicine has played a remarkable role to cure and preventing various diseases from ancient times. In the Unani system of medicine, rheumatoid arthritis is described under a broad discussion of waja'al-mafāsil, which is an Arabic term consisting of two words "waja'" meaning pain and "mafāsil" meaning joint. Waja'al-Mafāsil is also known as Hudār.^{10,11,12} Eminent Unani scholars of the past have elaborately described waja'al-mafāsil and managed with the multidimensional approach by the principle treatment modalities of Unani medicine that includes, Ilaj bi'l Ghidha (Dieto-therapy), Ilaj bi'l Dawa (Pharmacotherapy) and Ilaj bi'l Tadbir (Regimental therapy). Ancient Unani physicians have mentioned numerous safe and effective single herbal drugs and polyherbal formulations, which have been in use for RA management for ages. Still, most drugs have not been evaluated on scientific parameters and lack randomized clinical trials.

UNANI CONCEPT OF WAJA' AL-MAFĀSHIL (RA)

Renowned Unani scholars have defined the disease in many ways as follows;

According to Ibn Sīnā, waja'al-mafāshil is a clinical condition of pain with or without stiffness in one or more joint caused by the accumulation of ruṭūbat ghariba (foreign humour) in the joints.¹³ Ismāil Jurjānī has defined waja'al-mafāshil by stating that "when the morbid matter is accumulating in the organs of joints and produce pain and inflammation, it is called as waja'al-mafāshil".¹⁴ According to Zakariya Rāzī "Waja'al-Mafāshil is one of those disorders which occurs in recurrent or paroxysmal attacks and is caused by the accumulation of excessive fluid in the joint. He considered waja'al-mafāshil, niqris (gout), and 'irq al-nasa (Sciatica) as a disease of the same genus.^{15,16} Akbar Arzānī have described waja'al-mafāshil as pain and inflammation of joints of hands and feet. Sometimes pain occurs with or without inflammation of the joint.¹⁰ Samar qandi have elaborated waja'al-mafāshil as the pain and inflammation occurring in surrounding organs of the joints that is the inner membranes lining of synovium, ligaments, tendons, muscles, and membranes covering the muscles. Sometimes the overlying skin becomes inflamed and appears reddish, as well as the membrane covering the internal organs of the heart and lungs etc., gets affected by the causative matter of the disease. Occasionally it involves mandibles, spines, and auditory ossicles, and sometimes the condition becomes complicated that could not be diagnosed.¹¹

Predisposing Factors of Waja'al-Mafāshil (RA) As Per Unani Literature

Age: Waja'al-Mafāshil is found in all ages. Baghdādī have mentioned in his book Kitab al-Mukhtarāt fī'l Tibb that the onset is most frequent between 16 to 50 years.¹⁷

Female Gender: Young women mostly effected before 20 years of age,¹⁷ menopause, breastfeeding for a long time, childbirth complications are described as predisposing factors.^{11,18}

Season: Incidence increases in rabi (spring) season followed by kharīf (autumn).^{11,14,15,17,19} Cold and humid environment is favourable for the development of waja'al-mafāshil.²⁰

Genetic Factor: Genetic predisposition and hereditary pattern, usually of maternal origin, have been described.^{11,12,14,19,20}

Socioeconomic Status: Poor and labourers are most commonly affected.^{11,20}

Physical Work: Strenuous physical exercise, over-exhaustion, tiredness, and hard work.^{17,21}

Dietary Habits: Imbalance caused by inappropriate eating habits and drinking of excess amount of alcohol,^{14,15,17,18,22} drinking water on an empty stomach,^{17,19} and during the bath,^{10,14,17} non-vegetarian diet,^{11,17,18} overeating,^{14,17,18,19} habit of staying on a full stomach,²² excess use of the acidic substance,¹⁸ excessive intakes of sugar,¹⁵ and cold and moist diet,^{17,18} intake of indigestible and heavy food items,^{14,17,18} poor or imbalance diet in labourer work increase the risk.^{17,18}

Disease: Zuf al-hazm (Weak digestion) leads to the production of akhlāt khām (immature humour) that accumulates in joints,^{11,14,19,22} sozāk (gonorrhoea),^{11,17,18} improper management of qūlanj (intestinal colic) causes diversion of morbid material towards the joints and leads to accumulation of waste products in the joint,¹⁸ injuries,^{11,14,17,21} toxicity or toxins in the blood as in

case of common cold,^{14,17} specific fever or in syphilis causes derangements in blood,^{11,18} infectious disease and chronic diseases also precipitate the disease,¹⁸ pent up pus in the body that may be caused by rupture of abscess near the joint.¹⁷

Cessation of Habitual Evacuants: Giving up of habits such as purgation and vomiting, bleeding from haemorrhoids, menstruation, a bloodletting that is faṣḍ (venesection), etc. and tark-e-riyādat (discontinuation of exercise) leads to accumulation of excessive morbid matter in the joint.^{14,15,17,18,19,22}

Miscellaneous: Sedentary lifestyle, excessive coitus, exercise or coitus just after having meals, taking a bath after meals on a full stomach, being constantly in the state of intoxication and coitus in that state is strongly associated with the disease development, getting wet in the rain, sleeping in a wet place, wearing wet clothes for a long time or cold exposure. According to Ibn Sīnā, the psychic factor is riskier for disease development.^{10,11,13,15,17,18,19,22}

ETIOPATHOGENESIS OF WAJA' AL-MAFĀSHIL

Ibn Sīnā has described aetiopathogenesis of waja'al-mafāshil in detail. According to him, waja'al-mafāshil occurs due to asbāb-e-fa'ila (efficient or primary cause) and asbāb-e-munfa'ila (secondary reason).¹³ Asbāb-e-Fa'ila (efficient primary reason) includes those causes which are directly responsible for disease initiation and pathogenesis leading to joint pain, which are

Sū'-i-Mizāj (Altered Temperament): Sū'-i-Mizāj (Altered temperament) may be sāda (without the involvement of humours, causing only functional changes of articular tissue) or maddī (with humoral involvement resulting in organic changes in joints), mufrad or basīt (single) like rīh or murakkab (compound) composed of two, three or four akhlāt (humours) and it may be of a specific vital organ like the heart or generalized to the whole body. Sū'-i-Mizāj may be either hār multahib (inflammatory and heat-producing), bārid munjamid (refrigerant and consolidate derangement of temperament) or yābis munqabiz (desiccant and astringent derangement of temperament).²³ Pain is either due to sū'-i-mizāj mustahkam (persistently altered temperament),¹⁰ mainly caused by sū'-i-mizāj bārid (cold derangement).¹³

Madda-al-Fāsīdah (Morbid Material): Madda-al-Fāsīdah is dam (sanguine), dam-e-balghamī (phlegmatic sanguine), dam-e-ṣafrāwī (bilious sanguine), dam-e-saudāwī (melancholic sanguine), balgham (phlegm), sudda-e-balghamī khām (obstructive raw phlegmatic), murra-e-mufrat (simple bilious), safrā-e-balghamī (phlegmatic bile), middah (pus) and rīh-e-motashābika (pent up gas), ghair pukhta khūn (immature blood).^{10,13} According to Samarqandī, the causative matter of the disease is white mucoid with thick consistency as the secretion of the synovial membranes is rich in white and mucoid fluid, and according to Ibn Sīnā, the causative matter is similar to pus (rīm).¹¹

Asbāb-e-Munfa'ila (Secondary Cause): These are the causes that indirectly affect the joints and make them susceptible to accept the morbid material with their subsequent accumulation that results in organic and functional changes of the joints. These factors are also mentioned by Jurjānī, Baghdādī, and Arzānī as depicted in figure 1. Jurjānī have described that the joints possess features to attract the fluid (ruṭūbat) towards itself. Heat is produced by the joint movement, leading to fluid flow towards the joint as heat has a quality to attract the fluid. As per the Unani hypothesis, the joints have no absorption power (quwat-e-jāziba). Fluid absorption depends on the heat and significant components of the joint, i.e., bones, cartilage, and ligaments cold and dry

temperament. Hence, the fluid which enters the joint cannot be reabsorbed and thus accumulates in the joint spaces. It is also hypothesized that weakness in *quwat-e-hāzma wa dāfea* (digestive and excretory powers) of joints leads to accumulation

of decaying matter, consequently leading to disturbances in the joint function. The resultant fluid is putrefied into harmful products that induce *waja'al-mafāšil*.^{14,24} Schematic presentation of etiopathogenesis is depicted in figure 1.

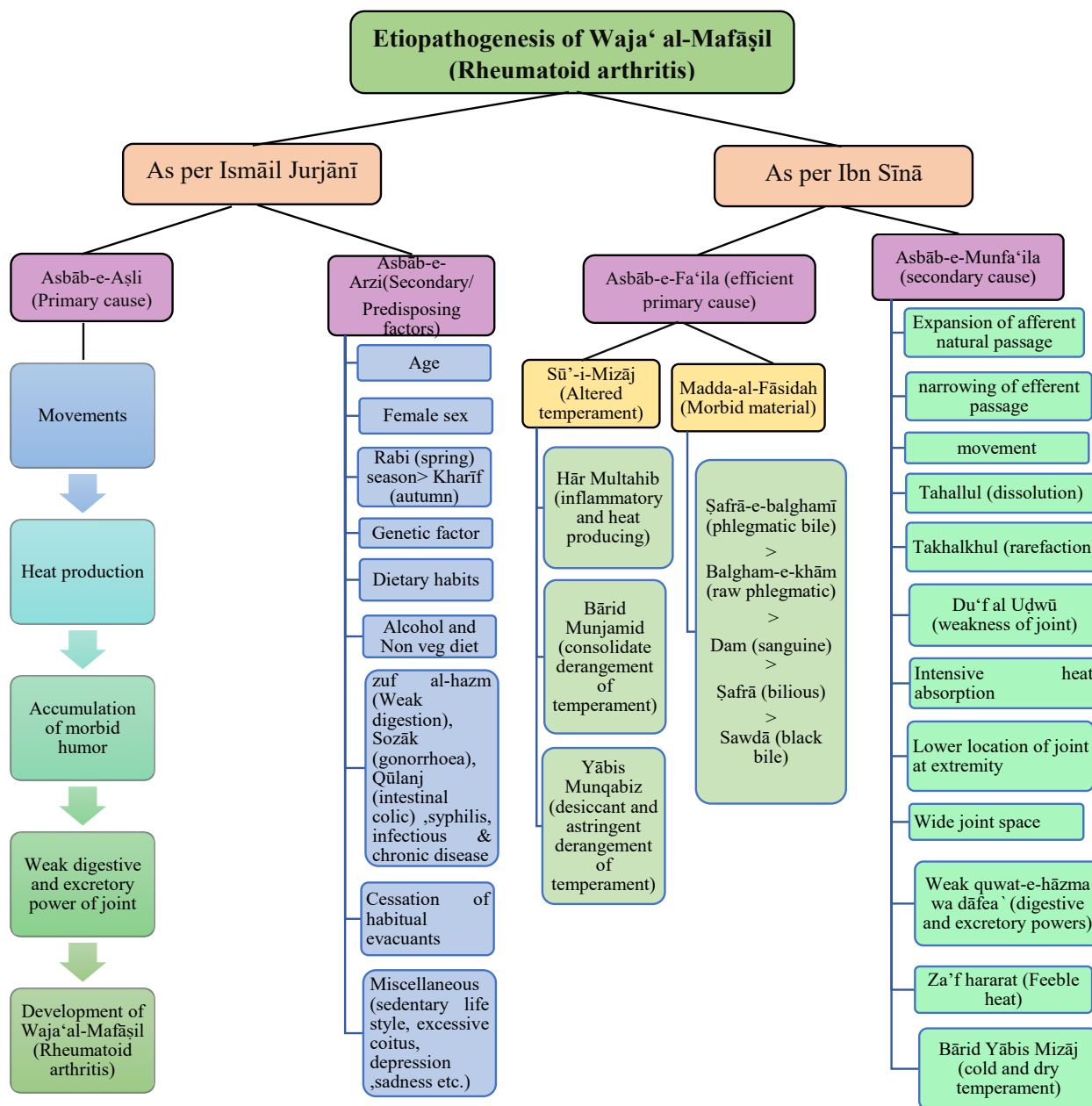


Figure 1: Schematic presentation of Etiopathogenesis of Waja' al-Mafāšil (RA)

Table 1: Types of Waja'al-Mafāšil^{10,11,17,18,21,23,35}

Types	Aetiology	Clinical Features	Reliving Factor	Diagnosis	Treatment Modalities
Waja'al-Mafāšil Sāda	Sū'-i-Mizāj Hār Sū'-i-Mizāj Bārid Sū'-i-Mizāj Yābis	Insidious onset, Mild pain, humoral congestion, no swelling	Exposure of substance opposite to altered temperament	Clinical, Type of sū'-i- mizāj is diagnosed by palpation, urine examination, pulse	Correction of altered temperament
Waja'al-Mafāšil Damwī (Plethoric)	Sanguine temperament, muscular body, use of haematinic syrup and food	Sudden onset, severe joint swelling, redness, severe throbbing, tenderness with tearing pain	Cold substances and fašd (venesection)	Warm affected joint but temperature not very high as compared to Şafrāwī(bilious)	Faşd (venesection), Muqqiyāt (emetics), Mus'hil (purgatives)

Waja' al-Mafāšil Šafrawī (Bilious)	Dominancy of šafra	Yellowish joint, severe pain with inflammation, burning sensation, heaviness and tingling, rapid pulse, fever	Cold exposure	Characteristics of predominant bilious humour, hot and dry temperament (šafrawī mizāj)	Istifrağh (evacuation), Naṭūl (irrigation), RM, Ḥammām (bath), DT
Waja' al-Mafāšil Balghamī (Phlegmatic)	Sudda-e-Balghamī Khām (obstructive raw phlegmatic), Safrā-e-Balghamī (phlegmatic bile)	Heaviness, mild pain, no warmth and burning sensation	Hot substances	Joint appear white, slackly with mild, soft, extensive swelling, cool on touch, other characteristics of predominant phlegm	MMT, Idrār-e-bawl (diuresis), DT
Waja' al-Mafāšil Sawdāwī (Melancholic)	The dominance of morbid sawdā	Joint appear blackish, mild pain, severe stiffness, tension and dryness on joint	Moist substances	Characteristics of excess melancholic humour, splenomegaly, skin cold on touch	Correction of spleen, Dalk (massage)
Waja' al-Mafāšil Rīhī	Rīh-e-Ghalīz (bad air)	Severe tension in joints, mild swelling and migratory pain	Evacuation of bad gases	Clinical	KR, DT, Takmīd (fomentation)
Waja' al-Mafāšil Murakkab	Alteration in more than one humours	Clinical features of two different types of causative humours	Not relieved by hot and cold temperament drug	In accordance with the dominant altered humour	MMT

MMT=Mundij-wa-Mus'hil Therapy (concoction and purgatives), DT=Ḍimād-wa-Tilā' (Medicated Paste and Liniment), RM= Riyādat Motadil (Moderate Exercise), KR= Kasir Riyah (Carminative) drugs

Table 2: Unani formulations Indicated in Waja' al-Mafāšil^{13,14,15,19,22,23,26,27,28,29,30,31,32,33,34}

Types of formulation	Name of Formulation
Arq	Arq Ushba
Ayarij	Ayarij-e-Harmas Ayarij-e-Faiqra Ayarij-e-Loghaziya Ayarij-e-Shabyar
Ḥabb	Ḥabb-e-Aafiat Ḥabb-e-Asgand Ḥabb-e-Suranjan Ḥabb-e-Ayarij Ḥabb-e-Azraqi, Ḥabb-e-Chobchini Ḥabb-e-Hudar Ḥabb-e-Irq-un-Nisa Ḥabb-e-Leemu Ḥabb-e-Sammul Far Musakkin Ḥabb-e-Mafasil Ḥabb-e-Gul-e-Aak Ḥabb-e-Astam Khiqūn Ḥabb-e-Baryuma Ḥabb-e-Muntin Akbar Ḥabb-e-Shītraj Ḥabb-e-Muqil
Halwa	Halwa Gheekwar
Itrifal	Itrifal-e-Muqil Mulaiyin
Jawāriḥ	Jawāriḥ Safarjali
Joshānda	Joshānda Suranjān and Bozidān
Kushta	Kushta Gaudanti
Ma'jūn	Ma'jūn Harmas Ma'jūn-e-Muddat-ul-Hayat Ma'jūn Musaffi-e-Azam Ma'jūn-e-Gheekawar Ma'jūn-e-Yahya Bin Khalid Ma'jūn Azaraqī Ma'jūn-e-Ushba, Ma'jūn Chobchini Ba Nuskha Kalan, Ma'jūn-e-Chobchini Ma'jūn-e-Falasisfa Ma'jūn-e-Jograj Guggul
Matbūkh	Matbūkh mufasil
Mufarreh	Mufarreh Sosambari
Safūf	Safūf Suranjān Safūf Suranjān Hakīm Sharif khān Safūf-e-Chobchini Safūf-e-Suranjan Zafrani
Tiryāq	Tiryāq-i-Arba' Tiryāq-i-Fārūq

Table 3: Clinical Studies for Waja' al-Mafāšil (RA) Management

Study Title	Study design	Intervention	Findings	Reference
Clinical Evaluation of Coded Drugs Unim-304 & Unim-312 Along With Munzij (Unim-308), Mushil (Unim-309) And Tabreed (Unim-310) Therapy in Waja-ul-Mafasil (Rheumatoid Arthritis)	An open-label clinical trial	UNIM-308; UNIM-309; UNIM-310;(MMT), UNIM-312: oral tablet, UNIM-304: Oil LA	Out of 55 cases, 21 cases got complete remission, 25 cases got remission partially, and 09 instances got poor remission	36
Therapeutic Effects of Eight Unani (Herbal) Drugs in the Patients of Waj-ul-Mafasil (Rheumatoid Arthritis) in the Development of Nuzj (Purgation) and Maintenance of pH of Urine - A Randomized Open Controlled Study	A randomized, open controlled study	Test drug-decoction of eight Unani (herbal) drugs Control drug-standard Unani pharmacopeial drug and Oil for LA.	Effective in recovery, development of nuzj (purgation) and maintenance of pH of urine between the ranges of 5 to 6.5 Nuzj started in urine by 2 nd week in 01(06.66%) patient, 03(20%) patients in 3 rd week, the sign of incomplete nuzj in 2 nd week, incomplete nuzj on 3 rd week in 3 patients, in 4 th week, out of 15 patients,	25

			12(80%) patients developed complete sign of nuzj with full turbidity in urine	
Multicentric Observational Studies of Polyherbal Unani Oral & Local Formulations in Cases of Rheumatoid Arthritis	Single-arm clinical study	MM therapy+ oral and local therapy of UNIM-301+302+304	Relieved pain and inflammations	37
Clinical Evaluation of Unani Drugs Majoon Suranjan, Safoof Suranjan and Raughan Suranjan in Waja-ul-Mafasil (Rheumatoid Arthritis) (A Preliminary Study)	Open clinical trial	Majoon Suranjan, Safoof Suranjan and Raughan Suranjan	Reduced joint pain, tenderness, morning stiffness, swelling, movement of restriction, muscular weakness= $p < 0.05$	38
A Clinical Study of Safety and Efficacy of Unani Pharmacopoeial Formulations of Habb-e-Suranjan and Raughan-e-Suranjan as Antiarthritic Effect in Waja-al-Mafasil (Joints Pain)	Single-arm clinical study	Habb-e-Suranjan and Raughan-e Suranjan	Joints pain, swelling, tenderness and restriction of movement= $p < 0.001$, no hepatotoxic, nephrotoxic effect	39
A Single Case Study of Rheumatoid Arthritis Under the Effect of Safoof Kundar (Powder of Boswellia Serrata)	Case Study	Powder of Boswellia Serrata), Rogni-e-surkh, fomentation: Trigonellauncata, Matricariachamomilla, Origanumvalgare	Reduced joint swelling, pain, morning stiffness, increase in haemoglobin level from 8gms/dl to 9.5gms/dl	40
Effect of Massage with Roghan Bishhapra (Oil of Trianthena Portulacastrum L.) in Rheumatoid Arthritis: Case Reports of Two Patients	Case Report	Massage with oil of Trianthena portulacastrum L.	Marked reduction in morning stiffness, pain and swelling	41
A case study in management of waja-ul-mafasil (rheumatoid arthritis) by Unani system of medicine	Observational single case design without a control group	Roghan-e-Surkh LA MMT x 18 days, Majoon Suranjan 7 gm & Majoon Azaraqi 5 gm BD, Habb-e-Suranjan 2 tabs TDS, Jawarish Shahi 5 gm OD, Habb-e Kabid Naushadri 2 tabs after a meal	Marked reduction in signs and symptoms (Severe to mild), Haemoglobin increased from 9.8 to 10.3 g/dl, RF reduced from 87.7 IU /ml to $\geq 32 < 64$ IU / ml	42

Table 4: Pre-clinical studies on Unani Formulations

Title of Study	Methodology	Intervention	Finding	Reference
Anti-inflammatory and antiarthritic activity of UNIM-301 (a polyherbal Unani formulation) in Wistar rats	Carrageenan-induced paw oedema and CFA induced animal arthritis models	Test: UNIM-301 in doses of 250, 500, and 1000 mg/kg BWT, Standard: Indomethacin 3 mg/kg BWT)	Reduced paw oedema and thickness, reduced serum pro-inflammatory cytokine levels viz. TNF- α , IL-1 β and IL-6 level in UNIM-301 group	43
Antiarthritic activity of Majoon Suranjan (a polyherbal Unani formulation) in rat	Turpentine oil-induced paw oedema, formaldehyde and complete Freund's adjuvant-induced arthritis models	Majoon Suranjan (in doses of 450, 900 and 1800 mg/kg BWT), standard drug-Aspirin (100 mg/kg BWT)	The antiarthritic activity of MS was due to the interplay between its anti-inflammatory and disease-modifying activities	44
Evaluation of therapeutic efficacy of Majoon Suranjan, an Unani formulation, in the treatment of rheumatoid arthritis: an experimental study	Efficacy-Arthritis induced male rats by immunization with bovine collagen type II, Safety-Acute and long-term toxicity studies	Methotrexate (0.25 mg/kg BWT, intraperitoneal once weekly) and MS (880 mg/kg BWT)	Majoon Suranjan is relatively safe and effective in decreasing the biomarkers of RA	45
Safety evaluation and therapeutic efficacy of Habb-e-Asgand, a commonly used antirheumatic polyherbal Unani formulation	Oral toxicity studies, collagen type II (CII)	HEA-57.5, 115, and 230 mg/kg BWT, methotrexate (MTX) at 0.25 mg/kg BWT	Safe- no overt toxicity or mortality, significantly reduced the levels of autoantibodies and CRP, comparable to MTX	46
Sub-chronic oral toxicity study of Habb-e-Suranjan in albino Wistar rats	Sub-chronic oral toxicity study	Habb-e-Suranjan at the dose levels of 2440 mg/kg of BWT	No incidences of mortality/morbidity, no significant difference in the body & organs weights, any hemato-biochemical & histopathological test	47
Majoon Ushba, a polyherbal compound, suppresses pro-inflammatory mediators and RANKL expression via modulating NF κ B and	Adjuvant-induced arthritis (AIA) rats	Majoon Ushba (100-300 μ g/ml)	Decrease in pro-inflammatory mediators (TNF- α , IL-1 β , IL-6, MCP-1, IL-17, iNOS, and COX-2) expression by suppressing NF κ B and MAPKs signalling pathways,	48

MAPKs signalling pathways in fibroblast-like synoviocytes from adjuvant-induced arthritic rats			significantly inhibited the level of lipid peroxidation, lysosomal enzymes release, and glycoproteins and increased antioxidant status	
Majoon Ushba, a polyherbal compound, ameliorates rheumatoid arthritis via regulating inflammatory and bone remodelling markers in rats	Complete Freund's adjuvant in Wistar albino rats	Majoon Ushba (1000 mg/kg/ BWT) and methotrexate (3 mg/kg/ BWT)	An increase in the level of cytokine (IL-10) inhibited overproduction of TNF- α , IL-1 β , IL-6, MCP-1, mRNA expression of TNF- α , IL-1 β , IL-6, IL-17, iNOS and COX-2, downregulated MCP-1, RANKL and transcription factors (NF- κ B and AP-1,) in synovial tissues, reduction in protein expression of NF- κ B, IL-17, COX-2, RANKL, OPG was elevated in synovial tissues, prevented body weight loss and reduced joint paw oedema, cell infiltration, cartilage and bone degradation	49
Evaluation of Anti-arthritis and Analgesic Effect of Unani Formulation Qurs-e-Mafasil Jadeed- A Preclinical Study	Freund's adjuvant arthritis test, Eddy's hot plate test and Analgesiometer test	Test drug: 2% aqueous suspension of test drug powder in gum acacia, Standard drug: Diclofenac	Decrease the hind paw volume and ankle joint thickness significantly (p<0.01)	50

RANKL=receptor activator of nuclear factor- κ B ligand, MCP-1=monocyte chemoattractant protein-1, iNOS=inducible nitric oxide synthase, COX-2=cyclo-oxygenase-2, OPG=osteoprotegerin, body weight: BWT

HOLISTIC APPROACH OF WAJA' AL-MAFĀŞIL (RA) MANAGEMENT

'Ilaj bi'l Ghidhā' (Dieto-therapy)

Ancient Unani physicians mention certain dietary recommendations and restrictions. According to Rāzī, bird meat and fish are beneficial in arthritis. Other dietary items recommended are wheat, pulses especially Bengal gram, Indian millet, big beans, French beans, spinach, onion, red chilli, black pepper, cumin, injīr (*Ficus carica* L.), bādām (*Prunus amygdalus* Batsch), pista (*Pistacia vera* L.), walnut, khajūr/ khurma (*Phoenix dactylifera* L.), apricot, grapes, potato, pure ghee, fenugreek, apple, papaya, masoor (*Lens culinaris* Medik), karnab (*Brassica oleracea* L.), cholai (amaranth), khurfa (*Portulaca oleracea* L.), chicken soup.^{10,15,19,22} All cold and phlegm-producing diets are restricted, as these diets minimize the effect of treatment and exacerbate the symptoms of RA. Rāzī has mentioned that meats are harmful and recommended vegetables. Restricted foods are fresh fruits, sour foods, meat, particularly cow and goat, alcohol, sweet dishes, carrot, cucumber, musk melon.^{10,15,22,23}

'Ilāj bi'l Dawā' (Pharmacotherapy)

Mundij-wa-Mus'hil Therapy (MMT) (Concoction and Purgatives): MMT helps in detoxification and excretion of morbid materials out of the body. Free radicals released by the neutrophils play an essential role in developing rheumatoid arthritis. They aggravate by decreasing "scavengers", which protect aerobic organisms against the harmful effects of free radicals in the joint cavity that mop up the free radicals. The free radicals may also be one of these morbid materials. Detoxification helps in eliminations of accumulated waste and fermenting bacteria from the digestive tract and stimulates the immune system.²⁵

Unani Formulations: A wide range of compound formulations that have been mentioned in classical Unani literature for the treatment of arthritis are displayed in table 2. Among these medicines, few have been proved safe and effective in RA management, depicted in table 3 & 4.

CONCLUSION

A vast experience-based pharmacological and non-pharmacological treatment methods have been used since antiquity. According to the Unani concept of waja'al-mafāşil, the causation of disease varies for different types of waja'al-mafāşil. By application of various hypotheses and treatment options available in ancient Unani literature, research may be needed to explore novel treatment modalities. There is only one RCT that has been done yet. The rest of the clinical trials have shown promising efficacy in the management of waja'al-mafāşil, but they are neither randomized nor well-designed. The scientific studies on Unani medicines have found safe and effective in animal models of RA with anti-inflammatory, analgesic, anti-arthritis, and disease-modifying activities. It may be concluded from this review that the need arises to conduct RCT with extensive design by using Unani formulation indicated in waja'al-mafāşil. Drugs in which pre-clinical study has done necessitate clinical research, and the non-randomized trials need to be evaluated on scientific parameters. Moreover, Extensive research can be conducted to exploit the unexplored potential of many other compound formulations and regimental procedures mentioned in classical literature.

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