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Concept of *Waja ál-Mafasil or Hudar* (Rheumatoid Arthritis) in Unani Medicine: A review

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Abstract
Rheumatoid arthritis (RA) is a long-standing inflammatory condition of undetermined causative factors with the hallmark of symmetric joint involvement. It is an autoimmune disease in which the body's immune system of the patient innocently targets its own body tissues. A principally attacks the synovial membrane, resulting in inflammation, proliferation, articular cartilage loss, and erosion of bone. The most prevalent inflammatory arthritic condition, rheumatoid arthritis (RA), affects 0.5% to 1% of the global population. It affects 15% (180 million) of the population of India. In the classical Unani literature, *Waja ál-mafasil* is described in detail for all types of arthritis, and one of its types *Hudar* has clinical features that are similar to those of Rheumatoid Arthritis (RA) which is mentioned in the modern system of medicine. According to the Unani System of medicine, *waja ál-mafasil* occurs in various joints caused by derangement of the body's natural humours i.e., *dam* (blood), *balgham* (phlegm), *safra* (bile), and *sauda* (black bile) with various explanations mentioned by great scholars in Unani literature. Contrary to modern management, which mostly relies on non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, and disease-modifying anti-rheumatic drugs (DMARDs), which come with many adverse effects, they managed it using a multidimensional approach. The main emphasis of this review article is on the important characteristics of rheumatoid arthritis with reference to *waja ál mafasil* to understand the status of the disease as described by Unani scholars and to offer a preferable option in terms of adverse effects and affordable treatment.

Keywords: *Waja ál-mafasil*, *Hudar*, Rheumatoid arthritis, Unani Medicine, Humours, *Ilaj-bit-Tadbeer*

Introduction
Rheumatoid arthritis is derived from the Greek word ῥεύμα-rheuma (nominative), ῥεύματος-'rheumatos'(genitive) ("flow, current")The translation is joint inflammation resembling rheumatic fever due to the suffix "oid," which means "resembling".'Rheuma' which translates to the watery discharge, may refer to the fact that the swollen joints or the disease are aggravated by the wet weather [11]. Rheumatoid arthritis (RA) is a long-lasting inflammatory condition of undetermined causative factors with the hallmark of symmetric joint involvement [1]. It is an autoimmune disorder characterized by the patient's immune system unintentionally attacking their own tissues in the body. Due to the synovial membrane being the primary target of RA, the synovium becomes inflamed and proliferates, articular cartilage is lost, and the bone is eroded [3]. However, aberrant systemic immunologic reactions are noticeable and may result in a number of extra-articular symptoms, including vasculitis, nodules, and accelerated atherosclerosis [2]. Combined, these conditions can shorten life expectancy by up to 10 years in severe cases [5]. It is a multifarious disorder due to its varying intensity, the unpredictable course of disease progression, and inconsistent therapeutic response. Even though the prevalence of RA varies geographically, this disease represents a significant global public health challenge. Mostly prevalent inflammatory arthritis, RA, affects 0.5% to 1% of persons globally [2]. The disease is also highly prevalent in India with a prevalence rate of 0.3–0.7% and it occurs more often in women than in men (female: male, 3:1) [7]. Despite substantial study and modern medical advancements, there is no long-lasting healing for RA. The main therapy goals are to lessen disease activity, establish remission, prevent joint damage, and improve the functional ability and overall well-being of the patient. Standard methods of medication like nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, Disease-modifying anti-rheumatic drugs (DMARDs), and biologics are effective but have a number of side effects. NSAIDs irritate the digestive tract, while long-term usage of corticosteroids can lead to peptic ulcers, osteoporosis, and delayed wound healing. DMARDs can have adverse effects that include liver and renal impairment. The immune system is suppressed by biologics, which causes bacterial and fungal infections.

Infection risk is increased by RA itself, along with DMARDs, and biological therapies, which also weaken the immune system through various pathways. Since ancient times, the Unani system of medicine has been incredibly effective in treating and preventing a wide range of diseases. *Waja ál-mafasil*, an Arabic term made up of the terms "*waja*" for pain and "*mafasil*" for joint, is used to explain rheumatoid arthritis in Unani medicine. *Waja ál-Mafasil* is also referred to as "*Hudar*."[16, 17] *Hudar* is a type of *waja ál mafasil* that has similar clinical features as Rheumatoid arthritis in the modern system of medicine. Depending on the type of *madda* affecting the joints, *Balgham* (phlegm) and *Sauda* (black bile) predominate, followed by *Safra* (bile), and very infrequently *Dam* (blood) is involved in *Hudar* (RA). There are occasions when more than one *khilt* (humour) is involved. The principle treatment modalities of Unani medicine include *Ilaj-bil-Ghiza* (Diet therapy), *Ilaj-bil-Dawa* (Pharmacotherapy), and *Ilaj-bil-Tadbeer* (Regimenal therapy) which have been extensively described and managed with a multidimensional approach by eminent Unani scholars in the past. Ancient Unani physicians have mentioned a variety of single herbal medications and polyherbal compositions that have been used for thousands of years to manage RA [6].

Unani Concept of *Wajaál-Mafasil*:

Ibn-e-Sina describes *waja ál-mafasil*, as a clinical condition marked by pain and stiffness in one or more joints brought on by the accumulation of *ratubat-e-ghariba* (foreign humour) in the joints [18]. *Zakariya Razi* states that "*Waja ál-Mafasil"* is a condition that manifests itself as repeated or paroxysmal episodes and is brought on by the accumulation of exaggerated fluid within the joint. He considered that gout, *Irq-un-nisa* (sciatica), and *waja ál-mafasil* all belongs to the same genus of disease [20]. *Ismail Jurjani* described *waja ál-mafasil* as such when morbid matter builds up in the organs of the joints and causes discomfort and inflammation [19]. *Waja ál-mafasil* is described by *Akbar Arzani* as discomfort in the hands and feet joints and inflammation. Pain can occasionally be present either with or without inflammation of the joint [16]. *Waja ál-mafasil* has been further defined by *Samar Qandi* as pain and inflammation in the tissues that surround joints, including the synovium, ligaments, tendons, muscles, and membranes that cover the muscles. Sometimes the disease's causative agent affects the membrane encasing internal organs such as the heart and lungs, causing them to become inflamed and appear reddish. Mandibles, spines, and auditory ossicles may occasionally be involved, and the problem grows so complex that a diagnosis is impossible [6, 17]. *Ibn Rushd* (1188 AD) in *Kitab-ul- Kulliyat* [22], *Rabban Tabri* (898 AD) in *Firdaws al-Hikma fi'l Tibb* [23], *Majoosi* (930 AD) in *Kamil al-Sana'a al-Tibbiyya* [24] discussed the disease in their treatise.

Classification of *Waja ál-Mafasil*

Renowned Unani specialists have categorized *waja ál-mafasil* based on a number of factors, some of which are listed below:

In accordance with the disease's severity

(a) *Haad* (Acute)
(b) *Muzmin* (Chronic)

In accordance with the presence of inflammation

(a) *Haar* (Hot) (with inflammation)
(b) *Barid* (Cold) (without inflammation)

In accordance with the etiology:

(a) *Waja ál-Mafasil Sada*
(b) *Waja ál-Mafasil Maddi*
(c) *Waja ál-Mafasil Reehi*
(d) *WajaálMafasilUfooni*

In accordance with the type of Madda (Morbid Substance)

(a) *Waja ál-Mafasil Damvi* (Sanguinous)
(b) *Waja ál- Mafasil Safrawi* (Bilious)
(c) *Waja ál-Mafasil Balghami* (Phelgmatic)
(d) *Waja ál-Mafasil Saudavi* (Melancholic)
(e) *Waja ál-Mafasil Murakkab* (Compound)

Further divisions of *Waja ál-Mafasil Murakkab* include:

(a) *Waja ál-Mafasil Safrawi Balghami*
(b) *Waja ál-Mafasil Safrawi Saudavi*

In accordance with the number of morbid substances present:

(a) *Mufrad*
(b) *Murakkab* [12]

In accordance with the occurrence of swelling: *Waja ál-*

(a) *Mafasil* is divided into the following categories by *Akbar Arzani*.
(b) *Dard ba warm* (*Waja ál-Mafasil* with swelling) (b) *Dard be warm* (*Waja ál-Mafasil* without swelling) [25]

In accordance with the accumulation of excessive abnormal fluids *(Akhlat-e-fasidah)*

Waja ál-mafasil may result from *Akhlat-e-fasidah* building up in the joint spaces, or it may just be a simple *waja ál-mafasil* (without accumulation of *Akhlat-e-fasidah*). Thus, *waja ál-mafasil* (especially of the chronic type) may be divided into two sorts according to the situation as follows: (a) *Hudar-e-Zulali* (Synovial type) (b) *Hudar-e-Azali* (Muscular type)

- ***Hudar-e-Zulali* (Synovial type)** which is also known as *Istisqa-e-Mafsali*, is characterized by an excessive accumulation of *ratubat-e-zulali* (synovial fluid) in the joint spaces, resulting in swelling, discomfort, and restricted joint movement.
- ***Hudar-e-Azali* (Muscular type)** is characterized by inflammation of the muscles that surround the joints without apparent fluid accumulation, causing the muscles to thicken, harden, and contract, resulting in painful joints [17].

In accordance with the joint involved

(a) *Irq-un-Nisa* (b) *Niqras* (c) *Waja ál-Zahr* (d) *Waja ál-Warik* (e) *Waja ál-Rukbah* (f) *Waja ál- Khasira (g) Waja ál-Saqain (h) Waja ál-Aqib*[10,12]

Etiology

Modern Aspect

Although the main etiology of RA is unknown, genes, environmental factors, and hormones may contribute to its onset and advancement. RA seems to be more likely in those who have certain risk factors, such as:

- Age (highest incidence among those 25 to 55 years old) [1]
- Gender (higher incidence in women)
- Genetics: RA is more prone to occur in those who were born with specific genes, especially human leukocyte antigen [HLA] class II genotypes, such as HLA-DRB1. In comparison to the general population, first-degree

relatives of patients are 2–10 times more likely to have RA.
- Smoking: Smoking and other bronchial irritants, such as exposure to silica, enhance a person's likelihood of acquiring rheumatoid arthritis if they carry the HLA-DR4 susceptibility allele because it increases the process of citrullination (conversion of arginine into citrulline) which lead to the production of ACPA (anti-citrullinated protein antibodies) is increased when smoking and HLA-DRB1 alleles are present simultaneously.
- Drinking coffee: Drinking coffee increases the risk of developing rheumatoid factor release. [21]
- APCA-positive people will develop rheumatoid arthritis in case of work exposure to silica. [21]
- Modifications in the composition and function of the gut microbiome have also been associated with rheumatoid arthritis. RA patients experience unhealthy gut and dysbiosis, a change in the gut microbiome's composition, whereby these patients have less diversity in their gut microbiota than healthy people. The genera *Actinobacteria*, *Collinsella*, *Eggerthalla*, and *Faecalibacterium* are increasing. *Collinsella* increases rheumatoid arthritis disease severity and modifies gut mucosal permeability. [15]
- The typical "western" diet, which is fatty, calorie-dense, and poor in fiber, raises the chance of developing RA. [15]
- Previous live birth data (higher RA risk with nulliparity)
- Early life exposures (If the mother smoked, the child has a greater incidence of developing RA).
- Patients who have rheumatoid factors (RFs) or anti-citrullinated protein antibodies (ACPAs) are also at a higher risk of developing RA [4].

Characteristics that can decrease the risk
- A larger intake of vitamin D, tea, oral contraceptives, a gluten-free diet, and breastfeeding can all lower the risk of developing rheumatoid arthritis [21].
- Long-chain omega-3 polyunsaturated fatty acid and antioxidant diet intake are linked to a decreased incidence of developing RA. [15]

Pathogenesis of Rheumatoid Arthritis

The pathologic process involved in RA are type 3 (immune complex) and type 4 (cell-mediated) reactions. Pathologic changes in RA pass through four stages:
1. Synovitis
2. Pannus formation
3. Fibrous ankylosis
4. Bony ankylosis

People having genetic factors like the HLA-DR4 gene located on chromosome 6, history or current viral infections like Epstein Barr virus, bacterial infection like Streptococcus, environmental factor like smoking (which increase the citrullination in the lung protein), and increase in citrullinated protein in the human body by enzyme PAD (Peptidyl Arginine Deaminase) activity in mucosal surfaces as well as in synovial fluid lead to activation of B-Cells which may trigger the activation of the immune system in rheumatoid arthritis.

Arginine amino acid is often found at the active site in proteins and enzymes due to its amine-containing side chain all over the body. Arginine may prevent or treat heart and circulatory diseases, combat fatigue, and stimulate the immune system.

Citrullination: It is the process of conversion of arginine (essential amino acid) into Citrulline (non-essential amino acid) by the enzyme Peptidyl Arginine Deaminase (PAD). Two isoforms, PAD 2 and 4 present in neutrophils and found in synovial fluid in RA patients.

In RA the immune system identifies the synovial membrane as foreign due to heavy citrullination in the synovial membrane (antigen-presenting cells) and being attacked by auto-antibodies (ACPAs) leading to the formation of the immune complex (antigen & antibodies complex) in the synovial membrane. Antigen-presenting cells (APC) are usually the macrophages that engulf the antigen resulting in the breakdown of the antigen into smaller particles by the enzyme (peroxidize) inside the APC. After that, the antigen is processed and transported to the surface of APC and then it binds to T-cells and becomes activated. APC secretes cytokines like Interleukin-I, Interferon-alpha, Interferon-gamma, and tumor necrosis factor. APC also secretes enzyme like lysozyme, elastases, and collagenases which causes the breakdown of cartilages.

On exposure to Interleukin-I synoviocytes proliferate and produce the following factors Interleukin-6 (IL-6), Prostaglandin-2, and platelet-activating factors which involve in the pain mechanism. Matrix metalloproteinase secretion leads to the activation of the collagenase enzyme responsible for the breakdown of cartilage.

Furthermore, the receptor activator of nuclear factor kappa B ligand (RANKL) is expressed by synoviocytes and lymphocytes to promote osteoclast development and activation. Proliferative and stratified synoviocyte-containing inflammatory granulation tissues grow till they come into contact with the bones. Multinucleated osteoclasts damage joints by destroying and absorbing bone, particularly at the site of contact. [31]

Etiopathogenesis of *Waja ál-Mafasil:* *Ibn-e-Sina* was the first to explain the etiopathogenesis of *waja ál-mafasil*, and other renowned physicians soon followed.

***Asbab-e-Faila* (Primary causes):** Refers to conditions whose pathophysiology and disease onset are directly related to joint pain.
- ***Su-e-Mizaj* (Derangement of temperament)**: *Su-e-Mizaj* can either be *sada* (producing only functional alterations in the articular tissue without the participation of humours) or *maddi* (with humoral involvement leading to organic alterations in joints). *mufrad* or *baseet* (single), such as *reeh*, or *murakkab* (compound), made up of two, three, or four *akhlat* (humours), and it may affect a single vital organ, such as the heart, or the entire body. *Su-e-Mizaj* can be either *haar multahib* (heat-producing and inflammatory), *barid munjamid* (refrigerant and consolidate temperamental disorder), or *yabis munqabiz* (desiccant and dehydrating). Either *su-e-mizaj mustahkam* (persistently unstable temperament) or *su-e-mizaj barid* (cold derangement) are the main causes of pain [6].
- ***Fasid Madda* (Morbid Substance):** *Fasid madda* is *dam* (sanguine), *dam-e-balghami* (phlegmatic sanguine), *dam-e-ṣafrawi* (bilious sanguine), *dam-e-saudawi* (melancholic sanguine), *balgham* (phlegm), *sudda-e-balghami kham* (obstructive raw phlegmatic), *mirra-e-mufrat* (simple bilious), *safra-e-balghami* (phlegmatic

bile), *middah* (pus) and *reeh-e-motashabika* (pent up gas), *ghair pukhta khoon* (immature blood). [16,18] *Samarqandi* claims that the disease's cause is thick white mucoid as the synovial membrane secretion is rich in white and mucoid fluid, while *Ibn-e-Sina* claims that the cause is similar to pus (*reem*). [13,17]

***Asbab-e- Munfailah* (Secondary causes)**: Factors that have an indirect impact on the joints and make them more prone to absorbing the morbid substance with their eventual collection, which causes alterations to the joints' structure and functionality. These factors are also indicated by *Jurjani, Baghdadi*, and *Arzani*. *Jurjani* has claimed that the joints contain characteristics that draw the fluid *(rutubat)* to themselves. The movement of the joint generates heat, which attracts fluid, causing it to flow toward the joint. According to the Unani concept, the joints cannot absorb energy *(quwat-e-jaziba).* The ability to absorb fluid is influenced by the heat and the cold and dry temperament of the bones, cartilage, and ligaments that make up the joint. As a result, fluid penetrates the joint but cannot be fully absorbed to collect in the joint spaces. Additionally, there is a theory that weakened joint *quwat-e-hazma wa dafea* (digestive and excretory powers) causes an accumulation of decomposing matter and, in turn, disturbs joint function. The resulting liquid is putrified into dangerous components that cause *waja ál-mafasil*. [6]

Clinical Features (*Alamaat*)

According to the type of etiology, several variants of *waja ál-mafasil* have different clinical traits, which are described below.

Waja ál-Mafasil Sada

This type is uncommon and lasts for a shorter period of time. It lacks swelling and *Imtila* (congestion) symptoms. The signs are alleviated by exposure to heat or cold. [12]

***Waja ál Mafasil Damvi* (Sanguineous)**

There are *Ghalba-e-Dam* (sanguine preponderance) symptoms present both generally and locally. The onset is relatively abrupt, and the symptoms and signs are severe. As the pain increases, the swelling becomes more obvious. Pain is throbbing in nature. Marked redness and warmth of the skin over the affected joint. Exacerbated by heat exposure and relieved by cold application or by venesection.

***Waja ál Mafasil Safravi* (Bilious)**

The presence of both generalized and localized signs of bile dominance (*Ghalba-e-Safra*). The skin above the joints has a faint yellow discoloration, which could also have a red tint. The swelling is less marked, with warmness compared to *waja ál mafasil damvi*, and throbbing pain over the joints are substantially worse. There is a desire for sour foods. Aggravated by heat and relieved by exposure to cold application across the affected portion.

***Waja ál Mafasil Balghami* (Phlegmatic)**

There will be both generalized and specific signs of phlegm dominance *(Ghalba-e- Balgham).* There is a gradual appearance of symptoms and signs. The damaged joint's area appears swollen, white, soft, and cold to the touch. There is mild pain and throbbing and the swelling is soft and cool. Aggravated by cold and relieved by applying heat to the affected part.

***Waja ál-Mafasil Saudavi* (Melancholic)**

The presence of both generalized and specific signs of the black bile *(Ghalba-e-Sauda)* dominance. On touch, the damaged joint area reveals a dusky, cold, and dry area. Sometimes the color changes to a bluish or purplish tinge. Aggravated by exposure to cold. The pain is less, and the swelling is moderate but stiff to the touch. Heat treatment over the afflicted portion can provide relief.

***Waja ál Mafasil Murakkab* (Involvement of compound/mixed humours)**

Waja ál-mafasil is a disease that can be brought on by any humour, although mixed humour can also do so. Pain and a combined clinical picture of all the relevant accumulating humours will be present. Heat or cold exposure can relieve symptoms.

***Waja ál-Mafasil Reehi* (Pneumatic):** It is a unique variety of *waja ál-mafasil*. Pain is light, doesn't feel heavy, shifts, and has a lot of distension.

***Waja ál-Mafasil Maddi*:** The affected joint appears extremely hot and itchy, tickly, and burning. Exposure to cold relieves symptoms, whereas exposure to heat makes them worse.

Complications and Fate of Disease: Depending on the quantity and severity of the morbid materials, as well as the chronicity of the disease, *Waja ál-Mafasil* may exacerbate a variety of disorders. Among the complications are joint abnormalities, dislocation, growth of nodules between joints, and *Tahajjur wa salabat-al-Mafasil* (ankylosis/joint stiffness with restricted movements). Even though they happen seldom, other systemic problems such as pericarditis, endocarditis, myocarditis, pneumonitis, pleurisy, tremors, chorea, and mania are possible. Meningitis, however, is the most serious form. [12]

Clinical Manifestations of RA: In most patients, pain, stiffness, and swelling in various joints develop slowly over a period of weeks to months. [3] Joint stiffness in the early morning persists for more than an hour and is alleviated by physical activity. The small joints in the hands and feet, are often the first joints to be affected symmetrically. The wrists, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints are the most affected joints. [1]

Articular Manifestations

- **Flexor tendon tenosynovitis** leads to decreased range of motion, reduced grip strength, and "trigger" fingers.
- **Ulnar deviation** results from subluxation of the MCP joints, with partial dislocation of the proximal phalanx to the volar side of the hand.
- **Swan-neck deformity** - Hyperextension of the PIP joint with flexion of the DIP joint.
- **Boutonniere deformity** -Flexion of the PIP joint with hyperextension of the DIP joint.
- **Z-line deformity**- subluxation of the first MCP joint with hyperextension of the first interphalangeal (IP) joint.
- **Piano-key movement** - Inflammation around the ulnar styloid and tenosynovitis of the extensor carpi ulnaris can cause subluxation of the distal ulna.
- **Pes planovalgus ("flat feet")** chronic ankle and metatarsal regions inflammation.
- Large joints, including the knees and shoulders, are often affected when the disease is present.

- Atlantoaxial cervical spine involvement may cause compressive myelopathy and neurological dysfunction. [1]

Constitutional symptoms are fatigue, weakness, low-grade fevers (≤38 °C), malaise, and depression.

Extraarticular manifestations: Subcutaneous nodules (30–40%), Secondary Sjogren's syndrome is the presence of either keratoconjunctivitis sicca (dry eyes), or xerostomia (dry mouth), Pleuritis, Pulmonary nodules, Pericarditis, Cardiomyopathy, Mitral regurgitation, Rheumatoid vasculitis, Anaemia, Felty's syndrome (neutropenia, splenomegaly, nodular RA) and Lymphoma [1].

Investigations: Complete blood count, Rheumatoid factor, Anti- CCP antibody, C- reactive protein, Erythrocyte sedimentation rate (ESR), MRI, Joint X-ray, Bone scan, Synovial fluid analysis, Antinuclear antibody (ANA) [9].

Treatment

The goals of treatment for RA include minimizing joint pain and inflammation, preventing joint destruction and deformity, maintaining the quality of life, and controlling extraarticular manifestations. Treatment regimens comprise combinations of pharmaceuticals, weight-bearing exercise, educating patients about the disease, and rest. Drugs used in the conventional system of medicine like Nonsteroidal anti-inflammatory drugs (NSAIDs), Corticosteroids (Methyl Prednisolone, Daflazocart), Disease-Modifying Antirheumatic Drugs (Methotrexate, Hydroxychloroquine, Sulfasalazine, Leflunomide), Biologics (Infliximab, Adalimumab) and Janus kinase (JAK) Inhibitors having a lot of adverse effects like gastritis, nephritis, osteoporosis, diabetes, hypertension, bone marrow suppression, leukopenia, hepatitis, rashes, etc. and in some condition to avoid permanent disabilities surgical interventions like arthroplasty and arthrodesis are advised. From the above description, it is the need of an hour to provide a safe and effective alternative treatment. [14]

Unani Management *(Usool-e-Ilaj):*

According to *Ibn-e-Sina*, the management of *waja ál-mafasil* should be diversion *(Imala-e-Mawad)* and evacuation *(Istefragh)* of morbid humours, *Munzij-wa-Mushil* (Concoctive and Purgative) therapy, strengthening of joints and its *Quwa* helps in restoring the joint in normal condition and prevent disabilities. In the Unani system of medicine, the main principles of management are, *Ilaj-bil-Ghiza* (Dietotherapy), *Ilaj bil Tadbeer* (Regimenal therapy) *Ilaj bil Dawa* (pharmacotherapy) for the management of *waja ál-mafasil* (RA).

***Ilaj-bil-Ghiza* (Dietotherapy)**

Zakaria Razi suggests that fish and poultry are favorable for *waja ál-mafasil* patients. Other foods that are advised include, particularly Bengal gram, Indian Millet, Big beans, French beans, Palak *(Spinacia olearacea* L.*)*, Pyaz *(Allium Cepa* L.*)*, Chuqandar *(Beta vulgaris* L.*)*, Carrot *(Daucus carota* L.*)*, Chilly *(Capsicum annum* L.*)*, black pepper *(Piper nigrum* L.*)*, Injeer *(Ficus carica* L.*)*, Badam *(Prunus amygdalus* L.*)*, Akhrot *(Juglans regia)*, Khajoor *(Phoenix dactylifera* L.*)*, Apricot, Angoor *(Vitis vinifera* L.*)*, Aaloo, Pure ghee, Methi *(Trigonella foenum* L.*)*, Shaljam *(Brassica rapa* L.*)*, Seb *(Malus sylvestris* L.*)*, Makka *(Zea Mays* L.*)*, Pineapple, Strawberry, and Papita *(Carica papaya* L.*)* [12].

Ilaj-*bil-Dawa* (Pharmacotherapy)

For Oral Administration

Single drugs *(Mufradat)*: Several single drugs are used in the Unani system of medicine like Suranjan *(Colchicum luteum* L.*)*, Asgandh *(Withania somnifera* L.*)*, Bozidan *(Tanacetum um- belliferum* L.*)*, Filfil Siyah *(Piper nigrum* L.*)*, Turbud *(Operculina terpethum* L.*)*, Zanjabeel *(Zingiber officinale* L.*)*, Sana Makki *(Cassia augustifolia* L.*)*, Mako *(Solanum nigrum* L.*)*, Halela Siyah *(Terminalia chebula* L.*)*, Kasni *(Chicorium intybus* L*)*, Badiyan *(Foeniculum vulgare* L.*)*, Gul-e Surkh *(Rosa Damascus* L.*)*, Elva/ Sibr *(Aloe barbadensis* L.*)*, Lufah *(Atropa belladona* L.*)*, Muqil *(Commiphora mukul* L.*)*, Qunturyoon *(Centauria centaurium* L.*)*, Qust *(Saussurealappa F.)*, Saqmonia *(Convolvulus scammonia* L.*)* and Shahatra *(Fumaria parviflora* L.*)* [27,30].

Compound Formulations *(Murakkabat)*: Several compound drugs are used in the Unani system of medicine like Majoon Jograj Gugul, Majoon Suranjan, Safuf Suranjan, Habb-e-Suranjan, Habb-e-Gul-e-Aakh, Habb-e-Asgandh, Habb-e-Azaraqi, Habb-e-Muntan, Habb-e-Najah, Habb-e-Sheetraj, Habb-e-Mafasil, Habb-e-Kuchla, Iyarij Faeqra, Jawarish Jalinoos, Jawarish Safarjali, Majoon Azaraqi, Majoon Chobchini, Majoon Najah, Majoon Safarjali, Majoon Ushba, Qurs Mafasil, Tiryaq-e-Kabir, Tiryaq-e- Arba' and Tiryaq-e-Farooque [28, 30].

Formulations for Local Application: Several formulations for local applications like Roghan-e-Malkangani, Roghan-e-Suranjan, Roghan-e-Chahar Barg, Roghan-e-Haft Barg, Roghan-e-Surkh, Roghan-e-Mafasil Roghan Hakeem Ajmal Khan, Roghan-e-Qust, Roghan-e-Marzanjosh, Roghan-e-Baboona, Roghan-e-Zaitoon, Roghan Badam, Roghan-e-Auja, Roghan-e-Chobchini, Roghan-e-Dhatura, Roghan-e-Balsan, Roghan-e-Satawri, Roghan-e-Jundaebedastar, Roghan-e-Gul-e-Aakh, Roghan-e-Kuchla, Roghan Mom, Roghan-e-Hanzal and Roghan-e-Sosan [30].

***Ilaj-bil-Tadbeer* (Regimenal therapy)**

***Hijama* (Cupping):** Dry cupping *(Hijama-bila-Shart)* is used for *Imala-e-mawad* (diversion of morbid material) while wet cupping *(Hijama-bil-Shart)* is used for *istefragh* (evacuation of morbid material). According to *Jalinoos*, *hijama* is useful in resolving *Ghaleez Khilt*. [9]

***Nutool* (Irrigation):** A revolutionary method called *Nutool* uses water, oil, or decoction of herbal drugs that are poured on certain body parts from a height to treat joint pain, improve local drug absorption, and help to deliver the intended local drug activity.

***Takmeed* (Hot fomentation):** *Takmeed* refers to the process of maintaining body temperature or the temperature of particular body areas. It is a therapeutic technique used to reduce stiffness and pain.

***Dalk* (Massage)**: It is a form of *Riyazat* (manipulation method) that strengthens ligaments and muscles, resolves and liquefies vitiated materials, and produces a small amount of heat [12].

***Bukhoor* (Steam fomentation):** *Bukhoor* is also very effective to reduce the symptoms of *waja ál-mafasil* (Rheumatoid Arthritis).

Recent Research

- Verma, et al., conducted a clinical study on the therapeutic efficacy of *Habb-e-Asgand*, an Unani compound medicine with anti-inflammatory, analgesic, and anti-rheumatic activity. They found that it significantly improved signs, symptoms, and C-reactive protein levels [8].
- According to reports, Suranjan Talkh *(Colchicum luteum)* is beneficial for treating a number of diseases, including *waja ál-mafasil* (rheumatoid arthritis). Colchicum luteum hydroalcoholic extract's antiarthritic properties were brought on by a modulating influence it had on the synovium's production of pro-inflammatory cytokines. It significantly reduced the swelling of joints in arthritis brought on by both formaldehyde and CFA (Complete Freund's adjuvant). The level of serum TNF-□ was also markedly decreased (Nair, et al., 2011) [32]. Similarly, *Colchicum luteum* proved beneficial effect on Javed. et al., clinical's study on the management of rheumatoid arthritis (RA). The medication appears to have analgesic and anti-inflammatory effects in RA, as it lessens or eliminates the disease's symptoms and signs [29].
- *Majoon Suranjan* was found to be effective in lowering the estimated levels of the RA biomarkers serum rheumatoid factor, anti-cyclic citrullinated peptide antibody, antinuclear antibody, and C-reactive protein when Subramaneyaan et al., conducted an experimental study in Wistar rats in 2013, this finding provided scientific support for the traditional use of *Majoon Suranjan* in the treatment of RA [26].

Conclusion: Rheumatoid arthritis is a chronic autoimmune disorder with the characteristic features of the destruction of synovial membranes, cartilage, and joints. The disease develops with pathological processes that are influenced by environmental and genetic factors. Rheumatoid arthritis is described in Unani medicine as *Hudar* which is a type of *waja ál-mafasil* that refers to a variety of joint disorders which includes inflammatory, non-inflammatory, infectious, metabolic, and other musculoskeletal disorders. The primary goal of treatment is to re-establish a healthy temperament and balance the *Khilt* (humour) through both *Imala* (diversion of morbid material) *Istefragh* (evacuation of morbid material). It can be said that the Unani method of treatment offers an alternative approach for RA both affordable and virtually without adverse impacts.

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