Are Traditional Remedies Useful in Management of Fibromyalgia and Chronic Fatigue Syndrome? A Review Study

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Abstract
Fibromyalgia and chronic fatigue syndrome are disorders that often occur simultaneously and are characterized by widespread pain and persistent fatigue. The patients are associated with disability and impairment social and physical functions. There are many remedies in traditional Persian medicine suggested for management of the disease complaints. The aim of this study was to investigate the clinical presentations and pathophysiology of disorders with the basic and principal textbook of traditional Persian medicine written by Avicenna (Canon of Medicine). According to Persian medicine, the term E‘aya can be matched by mentioned disorders. Avicenna believed that strenuous activities play an important role in the beginning of some types of fatigue. He classified fatigue into 4 groups, and in each type the clinical symptoms varied. The multifaceted entity of fibromyalgia and chronic fatigue syndrome in Persian medicine and conventional medicine suggests multidisciplinary therapies in management of these disabling disorders.

Keywords
fibromyalgia, fatigue syndrome, traditional medicine, complementary therapies, herbal medicine

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Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are disorders that often have comorbidities together and are characterized by widespread pain and disabling fatigue, respectively.1-3 The most common symptoms are memory problems, sleep disorders, psychiatric problems, muscle pain, feverishness, postexertional malaise, and headache.4-8 Musculoskeletal pain, fatigue, stiffness intensified by exercise, and postexertional weakness are common.9-11 Patients with FM may also suffer from a range of other disorders such as irritable bowel syndrome, cognitive dysfunction, restless legs syndrome, interstitial cystitis, and pelvic pain syndrome, but the prominent feature of FM is a musculoskeletal pain and tenderness that may be described as numbness, pricking, burning, and stabbing feeling. The patients also have sensory overload to cold temperatures.12,13

Fibromyalgia is one of the most common disorders that patients refer to physicians for primary care.9 Prevalence rates of FM were estimated between 2.1% and 5.3% in the general population, with a female preponderance regarding symptom severity.14,15 The period of FM is mostly chronic, but often symptom fluctuations are dependent on emotional distress.16,17 Both FM and CFS are more common in women.15,18,19 About 15 million persons in the United States suffer from FM. A total of 20% to 50% of FM patients have no acceptable efficiency in their routine affairs.20 These disorders are multifactorial and agents contributing the pathogenesis are considered as dysregulation of central nervous system, neurotransmitters and neuroendocrine disturbances, and physical trauma, including surgery, childbirth, and psychological characteristics.21 Although some remedial methods have been developed but there is no satisfactory cure for FM and CFS in conventional medicine. Pharmacological treatment including antidepressant agent, nonsteroidal anti-inflammatory drugs, sedatives, muscle relaxants, and antiepileptic drugs have been proposed. Because of insufficient treatments, nonpharmaceutical therapies such as cognitive behavior therapy, music, light aerobic exercise, and

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water-based exercise have also been recommended in patients with postexertional weakness.\textsuperscript{22-24} Drug therapy as the main rule for the management of patients with FM should be revised. Considering weak record of complete consumption of drugs by patients and high prevalence of adverse effects, the health care community must be carefully observe patients for both efficacy and complications.\textsuperscript{25} Recently, use of complementary and alternative medicine interventions has increased in chronic disorders. Some studies showed that 67.0\% of German FM patients used thermal baths, 35.2\% use different complementary medical interventions such as homeopathy, dietary supplements, and 18.4\% use meditative exercises such as yoga or Tai chi. Ultimately, every FM patient had used at least 1 complementary medicine therapy for this condition. Massage, acupuncture, yoga, and Tai Chi relaxation have shown promising effects in the treatment.\textsuperscript{26-28} Few trials on FM include biological outcomes, in particular as an assessment of inflammatory biomarkers. However, the association of neurogenic neuroinflammation with the pathogenesis of FM is proven.\textsuperscript{29} As mentioned, nonpharmacological treatments basically play an important role in the management of FM.\textsuperscript{13,22} According to the important role of complementary and alternative medicine to provide effective treatment in disabling illness, in this study we present the clinical manifestation, pathophysiology, and the treatment offered for FM and CFS in traditional Persian medicine.

Traditional Persian Medicine is the knowledge containing prevention, diagnosis, and elimination of diseases in Persia from ancient times and passed down from generation to present. According to traditional Persian medicine, health and disorder depend mainly on the condition of biochemical compositions. All normal body fluids and mediators are traditionally classified in 4 chemical groups, called Akhlat (humors), including Dam (blood or sanguine), Balgham (phlegm), Safra (yellow bile), and Soda (black bile).\textsuperscript{30-32} Each group contains many biochemical agents. Four qualifications, which are traditionally named “warmth,” “coldness,” “wetness,” and “dryness” represent metabolic aspects of each humor. For example, “warmth” is usually manifested by signs and symptoms such as heat sensation, good appetite, cordial and warm-blooded behavior, reddish skin, and high metabolic rate.\textsuperscript{33-35} Wetness and dryness are described as the spectrum of tissue moistures. Also, warmth and coldness are considered as a presentation of metabolic level.\textsuperscript{33} According to Avicenna, the signs of dominant sanguine are sensation of heaviness in the body, stretching, yawning and drowsiness. The other symptoms include disturbed senses, dullness in reasoning, fatigue sensation without any preceding exercise, and bleeding from the places which are easily ruptured like nostrils, anus, and gums. If the phlegm is dominant, some signs and symptoms could be observed such as excessive white color, flabbiness, soft and cold skin, abundant sticky saliva, and diminished thirst especially in old age, weakness of digestion, excess of sleep and sluggishness, laxity of nerves, and mental dullness.\textsuperscript{36} Changes in quantity or quality of humors disturb health state.\textsuperscript{36} Therefore FM and CFS can result from humor changes.

The aims of this study as a narrative review in Persian medicine literatures are

- Familiarity with traditional physician’s point of view about FM and CFS
- Finding some herbal remedies and non-pharmacological approaches to FM and CFS
- Opening a new window for future clinical trials

**Materials and Methods**

Reviews have been carried out in 2 fields, traditional Persian medicine and modern medicine. In Persian medicine, the most valid and famous basic textbooks that related to these chapters including Al-Qanun Fi al-Tibb, called Canon of Medicine in Latin (Ibn-e Sina, 980-1037 AD), Zahhrie Kharazmshahi (Jorjani, 1041-1136 AD), kamel-al-sanaeh al-Tebbiyeh (Ahvazi 930-994 AD), Makhzan-al-Advia (Aghili, 18th century) have been chosen according to experts’ opinion. The most common signs and symptoms of FM and CFS were extracted and compared with semiology of disorders in traditional literatures. The most compatible terms with FM and CFS in traditional Persian medicine were selected, including E’aya, Ta’ab, Kasalan, Seghl, Tahab-boj, and Tarrahol meaning fatigue, tiredness, contusion, heaviness, puffiness, and softening, respectively. Medline, Scopus, Google Scholar, and Iranmedex were also searched by keywords fibromyalgia, fatigue syndrome, traditional medicine, Persia, complementary therapies, herbal medicine from 2010 to 2016. Extracted materials were classified in definition, semiology, pathophysiology, and management.

A content analysis was carried out using software (MAXQDA.Plus v10.4.16.1), experts’ opinion, and professional consensus.

**Results**

*Ibn-e Sina (Avicenna)* believed that body functions were mainly carried out by biochemical components, traditionally called Akhlat or humors. All these chemical agents can be categorized into 4 groups, including blood or sanguine, phlegm, yellow bile, and black bile. Six etiologic categories, including climate, nutrition, sleep, physical exercise, waste disposal, and mental condition, which are called Setteh Zarourieh (meaning 6 necessary affairs) are responsible for health protection or disorder development. According to this point of view, for example, wet climate, overeating, cold and wet temperature foods and fruits (such as yogurt, watermelon, curd, potage, cucumber, sour dough), oversleeping, lack of exercise, and waste retention may lead to excessive cold and wet quality in body and this condition can result in disorders which are compatible with arthralgia, fatty liver, dyspepsia, gastroesophageal reflux, lower limb edema, constipation, weakness, and so on.

FM and CFS can be matched by some traditional terms such as E’aya meaning fatigue, Kasalan meaning broken sensation, and Ta’ab meaning physical tiredness. E’aya refers to boredom, fatigue, weariness, and harassment condition in Canon. *Avicenna* believed that some types of fatigue can be followed by excessive physical activity. He classified fatigue into 4
groups (1) E’aya Ghoruhi meaning ulcerous-sensed fatigue, (2) E’aya Varami meaning inflamed-sensed fatigue, (3) E’aya Tamaddodi meaning tension-sensed fatigue, and (4) E’aya Ghashafi meaning dry fatigue. Clinical symptoms and etiology are varied in each type. The important signs and symptoms of FM, CFS and their compatible traditional disorders have also been mentioned. According to traditional Persian medicine, fatigue treatment varies in every type of individuals but some recommendations are useable in all types. The fatigue that is caused by exercise does not appear if the exercise is stopped as soon as possible. The location of humor, maturity level, quantity and quality, and its viscosity are important in therapeutic protocol designing. For example, if the immature matter (excessive abnormal phlegm) is in the muscular tissues of the fatigued person, massage with increasing heat, maturates and changes it to warmer humors as a rheological change in matter for better application of the body, especially when the efficacy of the hot temperament medicines finds an access to it. Oil of dill (Anethum graveolens L), chamomile (Matricaria chamomilla L), and decoction of beet (Beta vulgaris L) root prepared with oils of the root of marshmallow (Althaea officinalis L), squirting cucumber (Ecballium elaterium), and wild vine (Bryonia alba) are also useful.

### Table 1. The Important Signs and Symptoms of Fibromyalgia, Chronic Fatigue Syndrome, and Their Compatible Traditional Disorders.1,37

| E’aya       | Fibromyalgia                                                                 | Chronic Fatigue Syndrome                                         | Drugs Offered in Traditional Persian Medicine                    |
|-------------|------------------------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|
| Ghoruhi (ulcerous): painful soreness or tingling by touching the skin, the movement increases pain sensitivity, painful stretching in limbs, fever and chill occurs if the pain be intensified | Abnormal muscle twitch response, muscle cramp, muscle weakness and fasciculation, generalized and localized stiffness that occurs in the morning and limited movement | Tender cervical and axillary lymph nodes, sore throat, myalgia, odynophagia, polyarthralgia, headache; unusual warm or cool extremities | Gentle massage with resolving oil such as chamomile, dill, root of marshmallow, beetroot, warm tub and lukewarm bath |
| Tamaddodi (tension): feeling heat, fullness and contusion in body or stretching in limbs, feeling heaviness or lightness, unrefreshing sleep | Boredom, fatigue, contusion feeling, unrefreshing sleeps insomnia, frequent nocturnal awakening, and restless leg syndrome, hypotonic or hypertonic muscle movement | Postexertional malaise and fatigue sleep disturbance, excessive day time sleepiness | Cumin, caraway, anise, gentle massage with resolving oil such as chamomile, dill, wormwood, and stinking bean trefoil |
| Varami (inflammatory): body is warm, full, and appears swollen, with a sense of tension | Hot and cold intolerance, persistent fatigue accompanied by impairment physical and mental function | Edema, feverishness, fatigue not improving with rest and resulting disability | Food and calorie restriction, drink coolers, topical use of sweet violet oil |
| Ghashafi (dry): feeling dryness and weakness in the body | Abnormal muscle twitch response, muscle cramp, muscle weakness and fasciculation, generalized and localized stiffness that occurs in the morning and limited movement | Tender cervical and axillary lymph nodes, sore throat, myalgia, odynophagia, polyarthralgia, headache; unusual warm or cool extremities | Gentle massage with resolving oil such as chamomile, dill, root of marshmallow, beetroot, warm tub and lukewarm bath |

E’aya Ghoruhi

If exercise is the sole cause in ulcerous fatigues, it must be reduced as soon as the fatigue appears. In some cases, the humors are excessive. In these conditions, the excessive humor should be eliminated by fasting, depletion, and dissolution. If the excess humor is near the skin it should be dispersed by excessive gentle massage with oil, having no contracting effect. Some moistening temperament foods should be given.

E’aya Tamaddodi

The aim in treating tension fatigue is to relax what has become rigid. This is to be achieved by gentle massage with oil warmed temperament in the sun and by sitting in bath with tepid water and the bath should be prolonged so much that even if it is taken twice or thrice a day, it is permissible. Oil should be rubbed after each bath. Then a small quantity of some moistening temperament foods should be given because in this type of fatigue, reduction of food is more needed than in ulcerous fatigue. This type of fatigue is relieved by exercise and sometimes even by itself. When fatigue arises spontaneously from excessive thick superfluities, depletion becomes essential. If it results from distending gases, it is relieved by cumin (Cuminum cyminum L), caraway (Carum carvi L), and anise (Pimpinella anisum L).

E’aya Varami

The aim of treating inflammatory fatigue is 3-fold: (1) relaxation of the distended tissues, (2) regimen for decreasing heat to reduce inflammation, and (3) depletion of superfluity. These aims are achieved by the following methods: (1) excessive application of warm oil, (2) very gentle massage, and (3) prolonged stay in warm tub or bath.
Table 2. Medicinal Plants Used for Management of Fibromyalgia and Chronic Fatigue Syndrome in Traditional Persian Medicine.38,39

| Scientific Names | Common English Name | Name(s) in Traditional Persian Medicine Literature | Family | Common Uses in Traditional Persian Medicine |
|------------------|---------------------|-----------------------------------------------|-------|-----------------------------------------|
| Althaea officinalis L. | Marshmallow | Khatmi | Malvaceae | E’aya, arteralga wound healer and respiratory diseases |
| Anethum graveolens L. | Dill | Shebet, shivid | Apiaceae | E’aya, arteralga, emenagoue and gastrointestinal disorders |
| Artemisia absinthium L. | Wormwood | Afsantin | Compositae | E’aya, arteralga, neurological disorders and gastric tonic |
| Beta vulgaris | Beet | Salgh, choghondar | Amaranthaceae | E’aya, arteralga, and skin disorders |
| Matricaria chamomilla L. | Chamomile | Babunaj, Babuneh | Compositae | E’aya, brain tonic, gastrointestinal disorder, and diuretic |
| Viola odorata L. | Sweet violet | Banafsaj, banafshe | Violaceae | E’aya, insomnia, and respiratory disorders |

E’aya Ghashafi

The treatment of dry fatigue is the same as that in the case of healthy persons. But the water for the patient of dry fatigue baths should be warmer.

Scientific, common English and traditional Iranian names of medicinal plants used in traditional Persian medicine for the management of FM and CFS are shown in Table 2.

Discussion

Some disorders in traditional Persian medicine are mainly compatible with conventional or modern medicine ones such as varicose, hemorrhoid, peptic ulcer, and so on. In many cases, this compatibility is controversial, for example, in diabetes mellitus, tuberculosis, and so forth. In these cases, comparison of signs and symptoms is more helpful. The most compatible disorder with FM and CFS, in traditional Persian medicine is E’aya. Etiology of FM and CFS in conventional medicine is not clearly known. In traditional Persian medicine, the most common type of E’aya was seen in moist and phlegm dominance. Many evidences in recent researches support this hypothesis, including:

- FM and CFS are more common in women (Ibn-e Sina stated that if sex is considered with reference to the difference of temperament, it is found that females are colder than the males, they are also more moist).
- Similarity in signs and symptoms: Ibn-e Sina has mentioned signs and symptoms for abnormal cold temperament such as deficient digestion, less desire for drinks, laxity of joint, excess of phlegmatic fever, discomfort from catarrh and taking cooling things, comfort and satisfaction from taking heat-producing things and the condition is worse in winter. Signs of abnormal moist temperament, including flow saliva and mucus, tendency toward diarrhea, dyspepsia, discomfort from taking moistening things, excess of sleep, and edema of the eyelids, which are common in patients with FM and CFS. FM and CFS patients have sensory overload to cold temperature. They also suffer from fatigue, malaise, irritable bowel syndrome, deep pain, numbness, cognitive dysfunction, which may be due to excessive moist (phlegm) in muscles, connective tissues, gastrointestinal system, ligaments, nerves, and brain, respectively.

Some complaints are similar in E’aya and autoimmune or rheumatologic syndromes. Specific involvement such as arthritis, aphtha, skin eruptions, esophagitis, and nephritis can be developed. FM and CFS are similar to E’aya from the viewpoint that there is no specific organ involvement. Most cases of E’aya are associated with retention. Retention of normal or abnormal biochemical components may lead to physical or chemical changes in humors and decreased basal metabolism rate, which are traditionally called Fesad and Boroudat, respectively. Most traditional interventions are directed toward increasing humor catabolism or excretion. Classification of E’aya or types of FM and CFS is based on the humor quality. Lifestyle changes, including dietary corrections, sleeping adjustment, proper physical activity, mental and emotional relaxation, and natural body wastes excretion are the principles of treatment protocol.40 Drugs such as cumin (Cuminum cyminum L), caraway (Carum carvi L), and anise (Pimpinella anisum L), physical methods such as massage with chamomile (Matricaria chamomilla L) and dill (Anethum graveolens L) oil are also recommended.38,40

Massage especially with resolving oils can reduce or dissolve the agents that affect muscles or ligaments. Some herbs that are listed in Table 2 reduce the moist humors in gastroentistinal or blood circulation and this may lead to decreasing in pathologic agents. Recent studies show anti-inflammatory and analgesic properties of chamomile (Matricaria chamomilla L) and dill (Anethum graveolens L). Phytochemical study of the aqueous extract of dill (Anethum graveolens L) demonstrates polyphenols, flavonoids, and tannins.41 One study confirms significant antidepressant and analgesic effect in rats compared with the drugs (sertraline and tramadol) without any adverse effects.42 Chamomile has anti-inflammatory activity by interfering with the cyclooxygenase pathway and active compounds including matricine, chamazulene, apigenin, bisabolol.43,44 Also, several studies show analgesic effect of chamomile in the arthralgia (carpal tunnel syndrome and knee osteoarthritis).45-47
Conclusion

FM and CFS can be largely matched by term E’aya in some aspects of traditional Persian medicine. Etiology of E’aya is somewhat inconsistent. It may be due to increased warm or cold, also increased or decreased humors. Treatment protocol is designed according to patient condition. The first step in therapeutic approach is temperament diagnosis and humor situation. Thus, in traditional approach, the patient plays a more important role than the disease. This concept has recently been called individualized medicine. Personalized or individualized medicine is a medical pattern that designs the health care protocol and medical decision for the individual patient. This point of view is one of the most important reasons for treatment plurality and multiplicity in traditional Persian medicine. Further clinical study should be performed to investigate this issue.

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Author Contributions

FM was involved with writing the article and data collection. RS gave the final approval to the study. MRN was involved with study design and data collection. MY was involved with conception, critical revision of article, and organization of funding.

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The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

This article is the result of a review study so no ethical approval is needed.

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