TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 10, Issue 2, Spring 2025

Review

Evaluation of Multiple Sclerosis from the Perspective of Conventional Medicine and Traditional Persian Medicine, Considering the Concept of Hemorheology

Mahdi Yaseliani[1], Hossein Rezaeizadeh[1], Abdolreaza Naser Moghadasi[2], Mohammad Ali Sahraian[2], Mehrdad Karimi[1], Mahdi Alizadeh Vaghasloo[1,3]*

[1]Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2]Multiple Sclerosis Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran
[3]Persian Medicine Network (PMN), Universal Scientific Education and Research Network (USERN), Tehran, Iran

Received: 8 Jul 2023 **Revised:** 21 Mar 2024 **Accepted:** 6 Apr 2024

Abstract

Multiple sclerosis (MS) is a persistent inflammatory disorder of uncertain etiology. Certain observations suggest that the pathology might not solely stem from primary immune dysregulation. Advanced imaging techniques reveal decreased cerebral blood flow in MS subjects compared to healthy controls, suggesting a widespread cerebral hypoperfusion present from early to advanced disease stages. One of the effective factors in reducing tissue perfusion is a change in the rheological properties of blood, which has been mentioned in recent articles. By attention to this concept in complementary and traditional medicine, including Persian medicine, this can be a common point that connects the view of Traditional Persian Medicine (TPM) on MS to the existing hypotheses about the role of hemorheology in the development of MS. For this study, a two-step literature search was conducted. The initial search focused on concepts related to MS disease and changes in blood consistency in most important TPM texts. For the second inquiry, the PubMed, ScienceDirect, Scopus, and Google Scholar databases were explored using the keywords related to MS and blood viscosity concepts. TPM, believes that the imbalance of the four Humors in the body, changes the physical properties of blood, leading to changes in the tissues blood supply and can cause nerve injury in the long run. On the other hand, in modern physiology, some evidence shows that circulatory disorders precede immune responses in the development of MS and the reaction of the immune system is actually secondary to the ischemia created as a result of reduced blood supply. We believe that discussing Hemorheology, not only in MS, but also in many other diseases, can open new horizons for knowing the root cause of the disease and thus discovering better treatments.

Keywords: Multiple Sclerosis; Traditional Persian medicine; Hemorheology

http://doi.org/10.18502/tim.v10i2.19062

Citation: Yaseliani M, Rezaeizadeh H, Naser Moghadasi A, Sahraian MA, Karimi M, Alizadeh Vaghasloo M. **Evaluation of Multiple Sclerosis from the Perspective of Conventional Medicine and Traditional Persian Medicine, Considering the Concept of Hemorheology**. Trad Integr Med 2025;10(2):162-167. http://doi.org/10.18502/tim.v10i2.19062

*Corresponding Author: Mahdi Alizadeh Vaghasloo
Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran
Email: mhdalizadeh@gmail.com

Introduction

Multiple sclerosis (MS) is a persistent inflammatory disorder of uncertain etiology [1,2], marked by immune-driven assaults on the central nervous system (CNS), leading to demyelination and harm to axons/neurons. The pathogenesis of MS is intricate, involving both T- and B-cell mechanisms, and its presentation is heterogeneous, with the underlying cause remaining unclear [3]. While the prevailing hypothesis attributes MS to an autoimmune process causing CNS myelin destruction [4], certain observations suggest that the pathology might not solely stem from primary immune dysregulation. Evidence indicates that plaque formation could have a basis other than destructive cell-mediated immunity targeting myelin or oligodendrocyte antigens [5,6]. Advanced imaging techniques, such as dynamic susceptibility contrast-enhanced perfusion magnetic resonance imaging (DSC-MRI) [7], reveal decreased cerebral blood flow in the normal-appearing white matter (NAWM) of MS subjects compared to healthy controls, suggesting a widespread cerebral hypoperfusion present from early to advanced disease stages [7-10].

One of the effective factors in reducing tissue perfusion is a change in the rheological properties of blood. Considering the importance of quantitative and qualitative changes in rheology in the pathogenesis of MS, which has been mentioned in recent articles and attention to this concept in complementary and traditional medicine, including Persian medicine [11,12], this can be a common point that connects the view of Traditional Persian Medicine (TPM) on MS to the existing hypotheses about the role of hemorheology in the development of MS, and we discuss this in this article.

Materials and Methods

For this study, a two-step literature search was conducted. The initial search focused on examining prominent texts related to MS in TPM to uncover the definitions and etiology of terms such as "*khadar*", "*Isterkha*", and "*Falej*".

In addition, words such as concentration (*ghelzat*), viscosity (*Lozujat*) and consistency (*Ghavam*) of blood and other body fluids were also searched. The Canon of medicine by Avicenna, Kamel-al-Sanaat al-Tibbiah (The Perfect Art of Medicine) by Majusi Ahwazi (Haly Abbas; 930- 994 A.D.), Al-Aghraz al-Tibb va al- Mabahes al- Alaieah and Zakhireh Kharazmshahi (Treasure of Kharazmshahi) by Jorjani (1042-1136 A.D.), Al-Mughni fi-l-Tibb: the sufficient of Medicine by Saeid ibn Hebatollah, and Exir-e-Azam (The great Elexir) by Hakim Azam Khan were among the most important TPM texts used in present review.

For the second inquiry, the PubMed, ScienceDirect, Scopus, and Google Scholar databases were explored using the keywords: "multiple sclerosis," "demyelination," "experimental autoimmune encephalomyelitis" (EAE), "autoimmune encephalomyelitis," and terms associated with blood viscosity concepts, including hemorheology, blood viscosity, and thixotropy.

Results

The concept of Hemorheology

The velocity of blood circulation within the blood vessels is influenced by various physical factors, such as the geometric and mechanical characteristics of the vessels, the force exerted by the heart to propel the flow, and the rheological attributes of the blood [13].

Microcirculatory failure can arise from insufficient perfusion pressure, vessel narrowing, or diminished blood fluidity [14].

The examination of flow behavior of materials or deformation is known as rheology [15] and hemorheology specifically pertains to the study of the flow characteristics of blood, including its plasma and cellular components. Blood viscosity is influenced by plasma viscosity, hematocrit, and the mechanical properties of red blood cells. Blood, behaving as a non-Newtonian fluid, exhibits variable viscosity with changing shear rates. At higher shear rates, such as those experienced during heightened blood flow, as seen in activities like exercise or peak-systole, blood becomes less viscous, exhibiting shear-thinning characteristics [16].

Role of Hemorheology in MS

Studies have shown that impaired tissue blood flow plays a key role in the development of neurodegenerative diseases. Widespread areas of hypoperfusion are known in Alzheimer (AD) and Parkinson disease compared with controls [17] and some experts propose the idea that AD might be triggered by inconspicuous and gradual ischemic episodes, silently impacting and slowly depriving individuals of their cognitive functions [18].

Specifically in MS, vascular congestion associated with thrombi in small veins and focal ischemic damage was considered to play a central role in the pathogenesis of CNS plaques.

In the context of MS, the involvement of vascular congestion, characterized by thrombi in small veins, and focal ischemic damage has been considered pivotal in the development of central nervous system plaques. The significance of blood and vasculature in the pathogenesis of MS plaques has been acknowledged for over a century, with Shulman et al. [19] referred to observations made by Rhindfleish in 1863 and Ribbert in 1882. Even in its initial phases, demyelination plaques form around minor veins, characterized by lower shear rates and elevated blood viscosity. The reduction in erythrocyte flexibility hampers blood flow in venules, leading to a further rise in blood viscosity

owing to the thixotropic properties of whole blood [20]. A research investigation involved the examination of rheological blood properties in 45 MS patients. Compared to the control group, the examined group exhibited increased plasma viscosity and accelerated red blood cell aggregation. Notably, 26.2% of patients displayed a significant rise in blood viscosity. These observed changes are believed to play a role in worsening microcirculation and exacerbating the demyelination process, as suggested by the findings [21].

In a separate investigation, females with MS exhibited elevated whole blood viscosity compared to controls at three out of four shear rates ($p < 0.001$). However, in males with MS, blood viscosity was higher only at a shear rate of 1.0 s^{-1} ($p < 0.05$). Proewig (1958) asserted that viscosity is notably elevated during the active phase of the disease but decreases during remissions [22]. Certain theories propose that the "lesion" in MS may stem from a fundamental rheological abnormality characterized by decreased flexibility of erythrocytes. According to the Poiseuille equation, abnormal blood rheology is anticipated to lead to stasis in the smallest veins where shear rates are lowest.

The subsequent decrease in microcirculatory flow may lead to tissue ischemia and harm. The inflammatory reaction to tissue damage could play a role in the abnormal permeability of the blood-brain barrier observed in MS [23,24] along with the edema commonly observed in initial lesions. This edema which is the result of poor tissue blood supply, appears to be a complication that can be traced back to other symptoms of MS such as visual problems.

Roizin et al. reported the occurrence of blood sludging in the conjunctival vessels of individuals with MS and proposed that this sludge might obstruct capillaries that supply nervous tissue. These observations of congestion, stasis, and sludging provide evidence for compromised microvascular blood flow in MS, a phenomenon that aligns with expectations if there is abnormal blood rheology [25].

MS equivalents and hemorheology in TPM

TPM, as one of the schools of humoral medicines, believes that "Humor" which is called in TPM texts as "Khelt" is a wet and fluid substance which foodstuffs in the first stage of permutation changes to it. Food undergoes various stages of digestion before transforming into Humor and reaching the tissues. These stages include gastric digestion, hepatic digestion, vascular digestion, and tissue digestion [26,27].

According to Al-Qanun fi al-Tibb, the blood and substances flowing within the vessels, result from the second stage of digestion [28]. Thus, an abnormal rise in blood viscosity resulting from irregular vascular content may be linked to dysfunction in one or both of the preceding digestion stages, specifically the hepatic and gastric digestion stages.

In the book "The Qanon of Medicine" by Avicenna, the foundation of TPM system was based on the balancing humors within the human body [29,30]. The disruption of this balance is associated with various diseases; while restoring equilibrium is linked to good health [29,30].

In the study of TPM, there are three diseases that are associated with MS in terms of signs and symptoms. Paresthesia and hypesthesia *(khadar*), weakness of the limbs of paresis (*Isterkha*), and paralysis (*Falej)* have some etiologies that are directly or indirectly related to the issue of blood flow and changes in the consistency of blood and other body fluids.

"*Khadar*" denotes the partial or complete absence of sensation in an organ [31,32]. It has multiple causes, with the most common one being a temporary restriction of nerve impulses to a specific area, often triggered by pressure or resting on body parts such as the legs. This is typically followed by a tingling sensation commonly described as "pins and needles" [33]. If for any reason the restriction continues, the nerves will be injured due to insufficient blood supply and the Paresthesia may continue even after the blood supply returns. With this description, changes in the tissues blood supply for any reasons other than external pressure can cause nerve injury in the long run.

Other important etiology of *"khadar*" is the change in the quality of body fluids and Humors. Excess abnormal temperaments such as Cold Excess OR Warm Excess OR Dry abnormal temperament generally affect the quality of the blood and then cause changes in the nerves.

Weakness of vital power which is actually the power of the heart is the other etiology of MS equivalents (in TPM texts) that is related to other cause of diminished tissue perfusion [34-36].

The most common concept of Paralysis (*Falej*) is the same type of paralysis caused by a stroke, and Avicenna describes various forms of "*falej*," such as monoplegia, hemiplegia, paraplegia, and quadriplegia. He underscores that the underlying causes in these cases are largely akin to those of "*khadar*" and "*isterkha,*" frequently intensified or occurring abruptly in this specific condition, and exacerbation of "*khadar*" may lead to "*falej"* or seizure, coma or cramps (spasms) [37].

Discussion

The role of blood rheology in the development of MS plaques has been acknowledged for over a century. Studies have shown that demyelination plaques are primarily located around small veins, where the shear rates are at their lowest and blood viscosity is at its highest [20].

As we are aware, the flow rates within blood vessels are influenced by various physical factors, such as the

geometric characteristics of the vessels, the pressure exerted by the heart to propel the flow, and, notably, the rheological properties of the blood under consideration [13].

The rheology of blood is related to features of the vessels and pressure power of the heart .As an illustration, blood viscosity decreases at high shear rates, such as those encountered during exercise or peak-systole. On the contrary, the viscosity of blood rises when shear rates decrease, for instance, in cases involving expanded vessel diameters or diminished flow, as seen downstream from an obstruction or during diastole [38]. Changes in blood consistency and viscosity is the source of a range of diseases from the perspective of TPM. TPM, as one of the schools of Humoral medicine, believes that the imbalance of the four Humors in the body, changes the physical properties of fluids in the body, especially blood.

From the perspective of TPM an important etiology of MS equivalents (in TPM texts) is change in the quality of body fluids and Humors which is known as dystemperaments with material .Also, excess abnormal qualities affecting temperaments such as Cold Excess due to side effects of herbal medications or opiate use OR Warm Excess due to fevers or a snake bite OR Dry abnormal temperament presenting as malfunction of the nerves is known as dystemperaments without material.

As another etiology, Avicenna says in the Canon of Medicine: The arrival of too much blood to the organs causes obstruction and finally leads to "*khadar*".

This type of functional obstruction caused by changes in blood characteristics is consistent with some evidence in conventional medicine about etiology of MS. This evidence suggests that circulatory disorders precede immune responses.

The generation of blood and its circulation from the heart through the vessels across the body appears to be a crucial factor influencing the creation and alteration of temperaments. In modern physiology, arterial blood is recognized for obtaining nutrients and chemical energy from the liver and lungs, along with receiving pressure and mechanical energy from the heart. It then disseminates these components throughout the entire body. Similarly, in TPM literature the blood is the vehicle of the "*Haar*" and heat. The "*Haar*" itself is the sum of the liver's natural spirit and the vital spirit of the heart [39].

Hence, the flow of blood plays a vital role in conveying both the mass and heat necessary for temperamental formation and the execution of tissue functions. It is explicitly mentioned that the body obtains its heat from the circulating sanguine and bile, that are the hot components of the blood [40].

This explains why organs with greater blood supply, like the heart and liver, are classified as warm-tempered; while those with lower blood supply, such as hair and bones are regarded as having cold temperaments. It also explains that why the lack of vital power in the organs, causes numbness in them and since the source of vital power is in the heart, it can be concluded that with the weakening of the heart, the shear stress caused by it is also reduced, and at lower shear stresses, the blood becomes more viscous and more difficult to penetrate into the tissues and this is the first step in the formation of MS plaques.

The clarification of treatment steps, conducted by Shirbeigi et al., emphasizes the importance of managing the common root causes of blood production and distribution. This differs from the practice of simultaneously prescribing various drugs for individual organ dystemperaments in a person. These explanations shed light on the fact that improving blood flow can correct dystemperaments and, consequently, address diseases caused by them. This underscores the role of hemorheology in the pathogenesis of diseases [41].

As mentioned in conventional medicine articles, during the progression of MS, edema can occur due to the abnormal permeability of the blood-brain barrier, resulting from an inflammatory reaction to ischemic tissue damage [23,24]. This edema which is the result of poor tissue blood supply, appears to be a complication that can be traced back to other symptoms of MS such as visual problems.

Averroes (Ibn Roshd, 1126-1198), an Arab physician from Andalusia, dedicates a particular chapter to disorders related to the sense of touch. In this section, he discusses inflammation of the optic nerve, a concept that closely aligns with optic neuritis (ON) in contemporary understanding. Averroes mentions that this condition is frequently associated with symptoms such as paresthesia and/or paresis in the limbs or face [42]. It is now acknowledged that ON is one of the visual system abnormalities observed in MS [43].

Avicenna initially outlines common causes for "*khadar*," emphasizing that an additional consequence of temperament imbalances associated with *khadar* and *isterkha* is the development of swelling or edema in the affected nerve sheaths. He notes that the accumulation of edema is a significant contributing factor to the progression of paresis [34-36]

In his Canon of Medicine, Avicenna provides a detailed account of transient blurred vision and blindness. Systematically, he lists possible causes linked to the visual system, including the eyes, nerve pathways, and the brain. In detailing the factors contributing to temporary blurred vision and blindness, he specifically highlights inflammation of the optic nerve, affecting both the nerve and axonal coverings. Consequently, this leads to swelling of the optic nerve and a decrease in optic nerve elasticity [43].

The most common concept of paralysis is the same

type of paralysis by strokes. As classified by Avicenna in the Canon of Medicine, various forms of paralysis—monoplegia, hemiplegia, paraplegia, and quadriplegia—may manifest. Avicenna also suggests that the underlying etiologies in these cases predominantly mirror those of *khadar* and *isterkha*, often intensifying or occurring abruptly [34-36,44].

However, in a specific subset of lesions exhibiting ring enhancement, elevated perfusion was observed solely in the ring tissue; while within the ring itself, there was a decrease in cerebral blood flow, indicating potential central ischemia [45]. Additionally, some individuals with MS form new plaques characterized by reduced mean diffusivity in MRI, akin to observations in acute ischemic stroke [46].

Macchi examined 100 plaques and observed infrequent occlusive lesions (thrombi). Nevertheless, he highlighted that the early phase of demyelination consistently involves stasis and congestion of venules and capillaries [47].

Further evidence supporting microcirculatory dysfunction in MS includes a reduction in cerebral blood flow, as indicated by xenon washout, and a significant association between diminishing cerebral blood flow and increasing disability [48].

Additionally, the systemic disruption of capillary blood flow serves as a foundation for comprehending other symptoms observed in MS patients, such as persistent fatigue [49], subcutaneous hemorrhage [50], sexual dysfunction [51] and cold extremities (unpublished observations).

In 1989, a novel diagnostic approach for MS was proposed, involving the determination of red cell suspension viscosity within the range of physiological temperatures. Three viscosity peaks (maxima) at 35, 37-38 (the physiological range), and 40 degrees Celsius have been identified, likely corresponding to thermotropic phase transitions in red cell membranes. The curves reflecting the dependence of eta (temperature degrees Celsius) in MS are indicative of the disease and may serve as a diagnostic test in laboratory settings [52].

From another perspective, improving the symptoms of MS patients following plasma replacement in some of its pathological types can suggest an effective role of plasma rheology in treatment [53].

Conclusion

This paper attempts to explore TPM manuscripts in an interdisciplinary effort, aiming to uncover potential insights on MS. It adopts a collaborative approach between conventional and traditional medical schools, specifically focusing on the field of hemorheology.

In this study, with the awareness of information shared by Rezaizadeh et al. indicating that a set of signs, symptoms, and etiologies identified in TPM manuscripts using terms like *khadar*, *isterkha*, and *falej* align with the symptoms and disease pattern observed in contemporary MS, we propose a theory. We conclude with a high probability that a shared pathological etiology may link the etiologies of MS in these two medical traditions.

We believe that discussing about Hemorheology, not only in MS, but also in many other diseases can open new horizons for knowing the root cause of the disease and thus, discovering better treatments.

Conflict of Interests

None.

Acknowledgements

None.

References

[1] Haki M, Al-Biati HA, Al-Tameemi ZS, Ali IS, Al-Hussaniy HA. Review of multiple sclerosis: epidemiology, etiology, pathophysiology, and treatment. Medicine 2024;103:e37297.

[2] Silva RV, Biskup K, Zabala-Jouvin JK, Batzdorf CS, Stellmach C, et al. Brain inflammation induces alterations in glycosaminoglycan metabolism and subsequent changes in CS-4S and hyaluronic acid. Int J Biol Macromol 2023;230:123214.

[3] Hunter SF. Overview and diagnosis of multiple sclerosis. Am J Manag Care 2016;22:s141-150.

[4] Ward M, Goldman MD. Epidemiology and pathophysiology of multiple sclerosis. Continuum 2022;28:988-1005.

[5] Henderson AP, Barnett MH, Parratt JD, Prineas JW. Multiple sclerosis: distribution of inflammatory cells in newly forming lesions. Ann Neurol 2009;66:739-753.

[6] Barnett MH, Prineas JW. Relapsing and remitting multiple sclerosis: pathology of the newly forming lesion. Ann Neurol 2004;55:458-468.

[7] D'haeseleer M, Hostenbach S, Peeters I, Sankari SE, Nagels G, et al. Cerebral hypoperfusion: a new pathophysiologic concept in multiple sclerosis?. J Cereb Blood Flow Metab 2015;35:1406-1410.

[8] Varga AW, Johnson G, Babb JS, Herbert J, Grossman RI, et al. White matter hemodynamic abnormalities precede sub-cortical gray matter changes in multiple sclerosis. J Neurol Sci 2009;282:28-33.

[9] Adhya S, Johnson G, Herbert J, Jaggi H, Babb JS, et al. Pattern of hemodynamic impairment in multiple sclerosis: dynamic susceptibility contrast perfusion MR imaging at 3.0 T. Neuroimage 2006;33:1029-1035.

[10] Law M, Saindane AM, Ge Y, Babb JS, Johnson G, et al. Microvascular abnormality in relapsing-remitting multiple sclerosis: perfusion MR imaging findings in normal-appearing white matter. Radiology 2004;231:645-652.

[11] Ibn Sina A. Al-qanun fit-tib [The canon of medicine]. Vol 2. Alaalami Beirut lib Press. Beirut 2005; p 331.

[12] Ibn Sina A. Al-qanun fit-tib [The canon of medicine]. Vol 2. Alaalami Beirut lib Press. Beirut 2005; p 311.

[13] Secomb TW, Pries AR. Basic principles of hemodynamics. Biomedical and Health Research-Commission of the European Communities Then IOS Press 2007;69:289.

[14] Isbister JP. Hyperviscosity: clinical disorders. biomedical and health research-commission of the european communities

Then IOS Press. 2007;69:371.
[15] Sousa PC, Pinho FT, Alves MA, Oliveira MS. A review of hemorheology: Measuring techniques and recent advances. Korea Aust Rheol J 2016;28:1-22.
[16] Baskurt OK, Meiselman HJ. Blood Rheology and Hemodynamics. Semin Thromb Hemost 2003;29:435-450.
[17] Heron CJ, Wright SL, Melzer TR, Myall DJ, MacAskill MR, et al. Comparing cerebral perfusion in Alzheimer's disease and Parkinson's disease dementia: an ASL-MRI study. J Cereb Blood Flow Metab 2014;34:964-970.
[18] Mazza M, Marano G, Traversi G, Bria P, Mazza S. Primary cerebral blood flow deficiency and Alzheimer's disease:shadows and lights. J Alzheimer's Dis 2011;23:375-389.
[19] Shulman MH, Alexander L, Ehrentheil OF, Gross R. Capillary resistance studies in multiple sclerosis. J Neuropathol Exp Neurol 1950;9:420-429.
[20] McMillan DE, Utterback NG, Baldridge JB. Thixotropy of blood and red blood cell suspensions. Biorheology 1980;17:445-454.
[21] Karlov VA, Savin AA, Smertina LP, Redchits EG, Seleznev AN, et al. Changes in rheological properties of blood in multiple sclerosis and their correction. Zh Nevropatol Psikhiatr Im S S Korsakova 1990;90:47-50.
[22] Blair GS, Matchett RH. Blood viscosity in multiple sclerosis. Journal of Neurology, Neurosurg Psychiatry 1972;35:730-371.
[23] Broman T. Supravital analysis of disorders in the cerebral vascular permeability II. Two cases of multiple sclerosis. Acta Psychiatr Scand 1947;22:58-71.
[24] Sears ES, Tindall RS, Zarnow H. Active multiple sclerosis: enhanced computerized tomographic imaging of lesions and the effect of corticosteroids. Arch Neurol 1978;35:426-434.
[25] Roizin L, Abell RC, Winn J. Preliminary studies of sludged blood in multiple sclerosis. Neurology 1953;3:250.
[26] Jorjani SI. Al-Aghraz al-Tibbia val Mabahess al-Alaiia. Tehran University Press. p 103.
[27] Arzani HMA. Medicine. In: institute ETT, 1 ed. Jalal al-Din. Qom 2008; p 15.
[28] Ibn Sina A. Al-qanun fit-tib [The canon of medicine]. Alaalami Beirut lib Press. Beirut 2005; p 48.
[29] Ibn Sina A. Al-qanun fit-tib [The canon of medicine]. Alaalami Beirut lib Press. Beirut 2005; p 46.
[30] Ahmad T, Anwar M. Clinical importance of leech therapy. Indian J Tradit Knowl 2009;8:443-445.
[31] Ahwazi A. Kamel-al-Sanaat al-Tibbiah. Vol 2. Jalaloddin. Qom 2008; p 365.
[32] Jorjani SE. Zakhireh Kharazmshahi (Treasure of Kharazmshahi). Vol 6. The lranian Culture Foundation. Tehran 1976; p 133.
[33] Gomatos Elias L, Scott C. Dulebohn, and Anis Rehman. "Sensory neuropathy." In StatPearls [Internet]. StatPearls Publishing 2024.
[34] Ibn Sina A. Al-qanun fit-tib [The canon of medicine]. Vol 1. Alaalami Beirut lib Press. Beirut 2005; pp 100-101.
[35] Azam Khan M. Exir Azam (Persian). Vol 1. Institute of Meical History, Islamic Medicine and Complementary Medicine. Tehran 2008. p 283.
[36] Jorjani SE. Zakhireh Kharazmshahi (Treasure of Kharazmshahi). The lranian Culture Foundation. Vol 1. Tehran 1976; p 171.
[37] Jorjani SI, Al-Aghraz al-Tibbia val Mabahess al-Alaiia. Tehran University Press. Tehran. p 491.
[38] Késmárky G, Kenyeres P, Rábai M, Tóth K. Plasma viscosity: a forgotten variable. Clin Hemorheol Microcirc 2008;39:243-246.
[39] Alizadeh Vaghasloo M, Naghizadeh A, Babashahi N. The concept of the Haar-re-Gharizi and Hararate Gharizi: The innate hot [Substance] and heat. Trad Integr Med 2017;2:3-8.
[40] Ibn Sina A. The Canon of Medicine. AlMayi. Vol 1. Tehran 2014; p 5; pp 67-71; p87; pp 301-304; p326; p362 [In Ara-bic].
[41] Shirbeigi L, Zarei A, Naghizadeh A, Vaghasloo MA. The concept of temperaments in traditional Persian medicine. Trad Integr Med 2017;2:143-156.
[42] Ibn Roshd, [Kulliyat or Colliget]. Dar al-kotob aliilmiyah: Lebanon 2005. p 141.
[43] Parviz M, Sahraian MA, Rezaeizadeh H. Historical issues of optic neuritis and sensory disorder in Persian traditional medicine. Iran J Public Health 2013;42:644.
[44] Saeid ibn Hebatollah, [Al-Mughni fi-l-Tibb: the sufficient of Medicine]. Dar Al-Nafaes press. Lebanon 1999.pp 65-59.
[45] Wuerfel J, Bellmann-Strobl J, Brunecker P, Aktas O, McFarland H, et al. Changes in cerebral perfusion precede plaque formation in multiple sclerosis: a longitudinal perfusion MRI study. Brain 2004;127:111-119.
[46] Rosso C, Remy P, Creange A, Brugieres P, Cesaro P, et al. Diffusion-weighted MR imaging characteristics of an acute strokelike form of multiple sclerosis. Am J Neuroradiol 2006;27:1006-1008.
[47] Macchi G. The pathology of the blood vessels in multiple sclerosis. J Neuropathol Exp Neurol 1954;13:378-384.
[48] Swank RL, Roth JG, Woody Jr DC. Cerebral blood flow and red cell delivery in normal subjects and in multiple sclerosis. Neurol Res 1983;5:37-59.
[49] Freal JE, Kraft GH, Coryell JK. Symptomatic fatigue in multiple sclerosis. Arch Phys Med Rehabil 1984;65:135-138.
[50] Swank RL. Subcutaneous hemorrhages in multiple sclerosis. Neurology 1958;8:497.
[51] Valleroy ML, Kraft GH. Sexual dysfunction in multiple sclerosis. Arch Phys Med Rehabil 1984;65:125-128.
[52] Ierusalimskiĭ AP, Kunitsyn VG, Nekrasova MF, Predtechenskaia AV, Chetvertakova TN. A rheological method of diagnosis of multiple sclerosis. Lab Delo 1989;10:39-41.
[53] Keegan M, König F, McClelland R, Brück W, Morales Y, et al. Relation between humoral pathological changes in multiple sclerosis and response to therapeutic plasma exchange. Lancet 2005;366:579-582.