

Available online at www.sciencedirect.com

Integrative Medicine Research

journal homepage: www.imr-journal.com

Review Article

New candidates for treatment and management of carpal tunnel syndrome based on the Persian Canon of Medicine



Mohammad Setayesh^a, Arman Zargaran^{b,c}, Amir Reza Sadeghifar^d, Mehdi Salehi^e, Hossein Rezaeizadeh^{f,*}

^a Department of Persian Medicine, School of Persian Medicine, Kerman University of Medical Sciences, Kerman, Iran

^b Department of Traditional Pharmacy, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

^c Department of History of Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran

^d Department of Orthopedic Surgery, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

^e Traditional and Complementary Medicine Research Center (TCMRC), Department of Traditional Medicine, School of Medicine, Arak University of Medical Sciences, Arak, Iran

^f Department of Persian Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:

Received 20 October 2017

Revised 6 February 2018

Accepted 13 February 2018

ABSTRACT

Carpal tunnel syndrome (CTS) is defined as a compressing median mononeuropathy. CTS is one of the major costly debilitating diseases of the hand. Although CTS is a relatively recent concept in current medicine, some evidences show that medieval physicians in Persian medicine (PM) such as Avicenna were familiar with it. The PM textbook written by Avicenna, the Canon of Medicine, defines the anatomy of carpal tunnel and median nerve, as well as mononeuropathy; it also offers suggestions for the prevention and treatment of carpal tunnel syndrome (called as *Vaja al-asab* and *Khadar*) in the chapter of nerve diseases. The book describes not only symptoms including pain, paresthesia, hypoesthesia, tingling, and numbness, but also its etiology such as nerve compression (entrapment neuropathy); nonphysical reasons such as disturbed balance among the four body humors; alteration in the nerve's temperament (*Mizaj*) that prevents the transmission of nerve impulses; and the others such as nutrition, mental condition, sleep, weather condition, body movements, and proper disposal of body waste. Furthermore, the book suggests a lifestyle modification method based on six factors and 10 prescriptions composed with 85 natural products that are not actively used for CTS treatment in modern times. The medicinal suggestions for CTS

Keywords:

Carpal tunnel syndrome

History of medicine

Neurology

Persian medicine

* Corresponding author. Department of Traditional Medicine, School of Traditional Medicine, Vafamanesh str., Heravi Sq. 1417653761, Iran.

E-mail address: rezaeizadeh@sina.tums.ac.ir (H. Rezaeizadeh).

<https://doi.org/10.1016/j.imr.2018.02.003>

2213-4220/© 2018 Korea Institute of Oriental Medicine. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

in the Canon of Medicine will be good candidates for discovering new treatments besides providing historical significance to the various insights considered 1000 years ago.

© 2018 Korea Institute of Oriental Medicine. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Carpal tunnel syndrome (CTS) is a clinical condition that is mainly characterized by sensory impairment (pain and paresthesia) in the median nerve of the hand.¹ CTS is the most common entrapment neuropathy at the wrist, and the prevalence of the disease is reported to be different in the general population, ranging from 3.8% to 16%. CTS is more common in females, during middle age, and in winter.^{2–8} This disease is also more common among employed individuals⁹ and is noted to be associated significantly with certain professions.^{10,11} CTS is the most common costly and debilitating disease of the upper extremity, and it is the cause for absenteeism from work for the most number of days, that is, up to 27 days.^{7,12–14} CTS is usually idiopathic; however, other diseases such as hypothyroidism,^{15,16} diabetes, rheumatoid arthritis, chronic renal failure, acromegaly, amyloidosis, hemophilia, gout, fracture and trauma in the carpal tunnel region, high BMI, pregnancy, and mitochondrial diseases^{17–19} can accelerate its development.⁷

Despite the developments in medicine, most supportive therapies in modern medicine, such as splinting and corticosteroids, do not have long-term effects even if they are helpful.^{7,20} Although surgical therapies have better long-term effects in reducing symptoms, patients are at risk of surgical complications. Overall, the available evidence supports the usage of nonsurgical treatments.²¹ Many studies have been conducted about the disease, but there is no consensus regarding the better options both in diagnostic and therapeutic methods.^{1,21} After pointing out the challenges in diagnosing and treating this disease, new ways to prevent the disease have been recommended.²¹

Being a good source to find new treatment approaches and remedies, the use of Traditional and Complementary Medicine (T&CM) is increasing rapidly in most countries, and the World Health Organization (WHO) recommends taking advantage of the capacities of traditional medicine due to its availability, affordability, and cultural acceptability.²² Moreover, healthcare workers are developing more positive attitudes toward T&CM.^{23,24} A serious reassessment of the traditional sources of medical information can be considered a postmodern approach to finding solutions to old unsolved problems.²⁵

Among the various traditional systems of medicine, Persian medicine (PM) is an ancient medical school that places great emphasis on disease prevention and lifestyle modification.²⁶ Persian physicians played a significant role in the development of medical sciences during the early medieval time (9–12th century AD). They followed the medical practices that were common in ancient Persia, India, Greece, and Rome.²⁷ This medical school gradually spread all over the

world, and important treatises, such as Avicenna's "the Canon of Medicine" (written in 1025 AD), were used as main medical textbooks in most eastern and western countries and medical centers until the 17th century.²⁸ Avicenna is one of the most prominent figures among the Persian physicians in that period. He had a great influence on the progress of medical sciences through history. He contributed significantly to the field of neurology and is known as a pioneer in this field.^{28,29}

Avicenna explains pressure on a branch of a nerve (compressive mononeuropathy), which is in accordance with the pathophysiology of CTS. In addition to recounting the etiology of nerve diseases and providing treatment options such as herbal and manual interventions, he offers a prevention package for these types of diseases. Therefore, this study aims to investigate Avicenna's views on neuropathy and carpal tunnel syndrome in his main medical textbook, *Canon of Medicine*.

2. Historical perspective

Classical history shows us that the term carpal tunnel syndrome (CTS) is not an old terminology in the history of medicine. Fothergill (1712–1780 AD) was the first man to describe the condition, which was later termed as neuralgia.³⁰ The first short description of patients with nocturnal hand pain, paresthesia, and weakness was published around 1850. The term acroparesthesia entered classic medical textbooks in around 1890, and the term CTS entered the literature in 1950. From the 1890s to the 1950s, acroparesthesia as a condition was described similar to what is today recognized as idiopathic CTS.³¹ Neuropathy was used in indexed medical articles for the first time in 1924.³² However, it seems that CTS was known by medieval physicians by other names and terminologies. Nerve-originated pain (*vaja al-asab*) was used as a term in medieval medical sources to define pain conditions. The term "Khadar" was also used by famous Persian physicians such as Rhazes (865–925 CE), Haly Abbas (949–982 CE), and Avicenna (980–1037 CE) to describe sensory impairment (e.g., numbness and paresthesia).³³

3. Avicenna (Ibn Sina)

Ibn Sina (980–1037 AD), who is known as Avicenna in western countries, was one of the greatest and most famous polymaths and physicians in the world. He played a great role in promotion of medicine in early medieval times.³⁰

Avicenna was born in Afshaneh (a city near Bukhara in the northeast of Old Persia). He finished learning Persian literature when he was 10 and became a famous physician when he was only 16 years old. He had more than 400 records in

Table 1 – Six essential factors in preventing neuropathies based on Avicenna's viewpoint

Essential factor	PM description and recommendations
Air	Air is a strengthening factor, which acts as a modifying and purifying agent in the human body. Air polluted with foreign particles throws the temperament off balance. Cold seasons make the neuropathy worse.
Rest and motion	Exercise is the most important factor in health promotion. Appropriate exercises (except repetitive hand movement) generate heat and gradually deplete the waste thick humors that influence the development of neuropathy. The appropriate exercise is that which starts mildly and then gradually becomes moderate; such exercise is the best option for the correction of nerve temperament after its purification (<i>tanghieh</i>).
Foods and drinks	Food management is the second most important factor after exercise for maintaining health. Sour foods, cold water, alcohol, foods requiring heavy and hard digestion (for example, cow meat, spaghetti, fatty sauce, fast foods, sausage, too fatty or fried foods, too cold and wet fruits), and the foods with cold temperaments are harmful to nerves. Dyspepsia leads to neuropathy.
Sleep and wakefulness	Effective sleep rejuvenates the body and prevents excessive depletion caused by immoderate movement and wakefulness. Sleep is quite similar to rest and wakefulness quite similar to the movement. Sleeping with a full stomach promotes the formation of nerve diseases.
Mental movement and repose	Lack of proportionality in any emotional state including anger, fear, sadness, happiness, etc., could disrupt the temperamental balance.
Evacuation and retention	Balanced depletion and retention of harmful and useful materials can prevent disease occurrence. Nerve depletion from the superfluous cold and thick (<i>bared – va – ghaliz</i>) substances, reinforce the nerve. Excessive sexual intercourse is harmful to the nerve.

the various fields of science such as philosophy, astronomy, and specially in medicine.²⁹ In the 12th century AD, his great medical manuscript, *Al-Qanun-fi-al-Tibb* (*The Canon of Medicine*), was translated into Latin by Gerard of Cremona. *The Canon of Medicine* was a comprehensive medical textbook consisting of five volumes that dealt with all aspects of medical sciences including basic sciences, diagnosis, anatomy, treatment, simple medicines registry, pharmacopeia, etc. The third volume of this book begins with neuroscience topics, including nerve diseases and its treatment approaches.^{28,33} Neurology is one of his favorite field of study. For example, he made pioneering discoveries in the field of vasovagal syncope,³³ migraine headache,³⁴ peripheral facial palsy,³⁵ and tremor.³⁶ He had also explained the management of stroke,³⁰ etc.

4. Carpal tunnel syndrome in Avicenna's Canon of Medicine

4.1. Anatomy of carpal tunnel and median nerve

In chapter 21 of the anatomy section of the *Canon of Medicine*, entitled “wrist (*rosgh*) anatomy,” Avicenna described the anatomic position of the carpal tunnel. Pinpointing the two rows of carpal bones and making explicit reference to the pisiform bone, he also noted the protective function of the carpal bones to let the only nerve pass through the concave surface of the carpal tunnel.³⁷

Avicenna has described cervical (*asab-al-onogh*) and thoracic (*asab-al-sadr*) spinal nerves. He also explained that brachial plexus is formed with the participation of some branches of the cervical nerves 5–8 (C5–C8) and the thoracic

nerve 1 (T1). Avicenna believed that the thoracic nerve 1 (T1) divides into two branches, and the second branch, which is smaller, merges with the cervical nerve 8 (C8) and extends to the hand to supply movement and sensation to the hand (median nerve).³⁷ Although generally what Avicenna described refers to general or focal functional distemperament of the patient, as well as changes in tissue and nerves passing through the tunnel, and not anatomical defects, his description of median nerve origination from the brachial plexus is fully compatible with today's anatomy.

4.2. Nerve diseases and CTS

In “the *Canon of Medicine*,” Avicenna explained that “the brain and spinal cord are the sources of nerve growth, and nerve function impairment can occur anywhere along its pathway.”³⁷ According to Avicenna's viewpoint, the onset of the symptoms of sensory and motor impairments can originate in the brain, the entire spinal cord, and a specific level of the spinal cord, or it can be due to mononeuropathy.³² He believed that the involvement of a branch of a single peripheral nerve (mononeuropathy) causes motor or sensory impairment within the same innervated organ.³⁷

In another general classification, Avicenna divided neuropathy into several distinct groups, namely sensory impairment [*Khadar*], paresis [*Esterkh*], paralysis [*Falej*], tremors [*Raasheh*], facial paralysis [*Laghve*], and spasms and muscle stiffness [*Tashannoj*].^{28,37}

In Persian medicine, *khadar* (sensory neuropathy) is a general term for a group of diseases that have similar sensory impairment symptoms such as pain, paresthesia, and

Table 2 – Medicinal plants in the Canon of Medicine for sensory neuropathy

Scientific name	Family	English common name	Traditional Persian name	Part use	Root of administration	Pharmacological effect ^a /type of study
<i>Brassica nigra</i> (L.) K. Koch	Brassicaceae	Mustard	Khardel	Seed	Topical	AI, AO, AG/in vitro ³⁸
<i>Costus</i> sp.	Costaceae	Costus	Ghost	Root	Topical (oil)	AI, AO/in vitro ³⁹
<i>Trifolium aureum</i> Pollich	Leguminosae	Large trefoil	Khandaghoghi	Leaf and Seed	Topical (oil)	-
<i>Medicago sativa</i> L.	Leguminosae	Alfalfa	Ratbeh (ghat)	Aerial parts	Topical (oil)	AO, AI/in vitro and in vivo ^{40,41}
<i>Scolopendrium vulgare</i> Sm.	Aspleniaceae	Hart's-tongue	Osghologhanderion	Leaf	Oral	-
<i>Ruta graveolens</i> L.	Rutaceae	Common rue	Sodab	Leaf	Oral	AO, AI/in vivo ⁴²
<i>Agrimonia eupatoria</i> L.	Rosaceae	Agrimony	Ghaafeth	Aerial parts	Oral	AO, AI/in vivo ⁴³
<i>Anemone coronaria</i> L.	Ranunculaceae	Anemone	Gole baad	Aerial parts	Oral and topical	AO/in vitro ⁴⁴
<i>Lawsonia inermis</i> L.	Lythraceae	Henna	Hana	leaf	Oral and topical	AO, AI, AG/in vivo ⁴⁵
<i>Acorus calamus</i> L.	Acoraceae	Sweet flag	Vaj	Root	Oral and topical	AO/in vivo ⁴⁶
<i>Pinus sylvestris</i> L.	Pinaceae	Pine	Senobar (kaaj)	Fruit	Oral	AO/in vitro ⁴⁷
<i>Nepeta menthoides</i> Boiss. & Buhse	Lamiaceae	Lavender	Ostokhoddus	Aerial parts	Oral	AO, AI/in vivo ⁴⁸
<i>Allium sativum</i> L.	Amaryllidaceae	Garlic	Sir (Soom)	Root	Oral and topical	AO, AG/Human study ^{49,50}
<i>Pimpinella anisum</i> L.	Apiaceae	Anise	Anisun	Fruit	Oral and topical	AO/in vitro ⁵¹
<i>Asarum europaeum</i> L.	Aristolochiaceae	Asarabacca	Asarun	Root-leaf	Oral and topical	AO/in vitro ⁵²
<i>Matricaria chamomilla</i> L.	Asteraceae	Chamomile	Babooneh	Aerial parts	Oral and topical	AO, AI/Human study ⁵³
<i>Colchicum autumnale</i> L.	Colchicaceae	Meadow saffron	Suranjan	Flower-Seed	Oral and topical	AI/in vivo ⁵⁴
<i>Cynara cardunculus</i> L.	Asteraceae	Artichoke	Kangar	Aerial parts	Oral and topical	AI/in vivo ⁵⁵
<i>Elettaria cardamomum</i> (L.) Maton	Zingiberaceae	Cardamom	Ghagholeh (Hel)	Fruit	Oral and topical	AO/in vivo ⁵⁶
<i>Lactuca sativa</i> L.	Asteraceae	Lettuce	Kahoo	Seed	Oral and topical	AO, AI, AG/in vitro ⁵⁷
<i>Marrubium vulgare</i> L.	Lamiaceae	Marrubium	Frasion	Leaf	Oral and topical	AO/in vitro ⁵⁸
<i>Morus alba</i> L.	Moraceae	White mulberry	Toote sefid	Aerial parts/Root	Oral and topical	AI, AO/in vitro - in vivo ⁵⁹
<i>Papaver somniferum</i> L.	Papaveraceae	Opium poppy	Khashkhaash	Flower	Oral and topical	AO/in vitro ⁶⁰
<i>Rosa Damascena</i> Mill.	Rosaceae	Rose	Vard Ahmar (Gol-e-Sorkh)	Flower	Topical (oil)	AO, AI, AG/in vitro and in vivo ⁶¹
<i>Taxus baccata</i> L.	Taxaceae	Yew tree	Sorkhdaar	Aerial parts	Oral and topical	AO/in vitro ⁶²
<i>Trigonella foenum graecum</i> L.	Fabaceae	Fenugreek	Shanbalileh	Seed	Oral and topical	AO, AI/in vivo ⁶³
<i>Olea europaea</i> L.	Oleaceae	Olive	Zeytoon	Fruit oil, leaf	Topical (oil)	AO, AI, NP/Human study ^{64,65}
<i>Linum usitatissimum</i> L.	Linaceae	Linseed	Katan	Seed	Topical (oil)	AO, AI, NP/Human study ⁶⁶
<i>Citrullus colocynthis</i> (L.) Schard.	Cucurbitaceae	Colocynth	Hanzal	Fruit	Oral and topical	AO, AI, NP/Human study ⁶⁷
<i>Veratrum album</i> L.	Melanthiaceae	White hellebore	kharbagh	Root	Oral	AO/in vitro ⁶⁸
<i>Euphorbia resinifera</i> O. Berg.	Euphorbiaceae	Spurge	Farfion	Gum	Oral	AI/in vitro ⁶⁹
<i>Ferula persica</i> Willd.	Apiaceae	Ferula	Sakbinaj	Gum	Oral	AO/in vitro ⁷⁰
<i>Dorema ammoniacum</i> D. Don.	Apiaceae	Ammoniac Gum	Oshagh	Gum	Oral and topical	NP/in vitro ⁷¹

^a AO: antioxidant; AI: anti-inflammatory; AG: analgesic; NP: neuroprotective.

hypoesthesia. *Khadar* can occur in one organ due to peripheral neuropathy, just like what occurs in CTS. In Avicenna's opinion, motor and sensory nerves are different in terms of texture and nature, which is called "temperament" in Persian medicine. Therefore, nerves are different in terms of acceptance of the disease, and sensory symptoms develop

before motor symptoms. Avicenna emphasized that as the causative agent becomes stronger, motor symptoms can be added to sensory symptoms, which is consistent with the process occurring in CTS. CTS is the peripheral neuropathy of the median nerve, wherein sensory symptoms, such as pain, paresthesia, hypoesthesia, tingling, and numbness, usually

Table 3 – Compound medicines in the Canon of Medicine for sensory neuropathy

Name of compound medicine	Dosage form	Ingredients	Chief virtue of the compound based on original text*	Volume/pages of source (Canon)
Dohn al-Qest	Oil	<i>Commiphora myrrha,</i> <i>Cinnamomum iners,</i> <i>Teucrium montanum</i>	Disentangling nerves obstructions	Volume 4/p. 541
Dohn-e Hendi	Oil	<i>Cydonia indica,</i> <i>Acorus calamus,</i> <i>Lepidium latifolium,</i> <i>Iris florentina,</i> <i>Inula helenium,</i> <i>Zingiber zerumbet,</i> <i>Piper longum,</i> <i>Strychnos nux-vomica,</i> <i>Trichilia emetic,</i> <i>Cupressus sempervirens,</i> <i>Populus,</i> <i>Costus sp.,</i> <i>Foeniculum vulgare,</i> <i>Cedrus deodara,</i> <i>Doronicum pardalianches</i>	Analgesic for pain due to dense cold gas and humor in nerves	Volume 4/p. 544
Dohn al-zafran	Oil	<i>Crocus sativus,</i> <i>Commiphora myrrha,</i> <i>Lagoecia cuminoides</i>	Softening stiffness (inflammation) of nerves	Volume 4/p. 545
Dohn-e Ofarbion	Oil	<i>Costus sp.,</i> <i>Commiphora myrrha,</i> <i>Castoreum,</i> <i>Mentha pulegium,</i> <i>Anacyclus pyrethrum,</i> <i>Gypsophila struthium,</i> <i>Cheiranthus cheiri,</i> <i>Iris florentina,</i> <i>Euphorbia sp.</i>	Analgesic for cold nerves pain	Volume 4/p. 545
Dohn-e Damamoon	Oil	<i>Liquidambar orientalis,</i> <i>Pistacia lentiscus,</i> <i>Cinnamomum tamala,</i> <i>Valeriana dioscorides,</i> <i>Euphorbia sp.,</i> <i>Cinnamomum zeylanicum,</i> <i>Apis mellifica,</i> <i>Moringa Arabica,</i> <i>Moringa pterygosperma,</i> <i>Commiphora opobalsamum,</i> <i>Piper nigrum</i>	Preventing bad humors and materials to nerves and softening of the nerves	Volume 4/p. 545
Saoot	Snuff	<i>Citrullus colocynthis,</i> <i>Beta vulgaris,</i> <i>Medicago sativa,</i> <i>Nigella sativa,</i> <i>Peganum harmala</i>	Efficient for cold pains and organ paresis; disentangling obstructions due to coldness and humidity in nerves	Volume 4/p. 565
Ethanasia al-Kobra	Electuary	<i>Crocus sativus,</i> <i>Commiphora myrrha,</i> <i>Papaver somniferum,</i> <i>Castoreum,</i> <i>Hyoscyamus albus,</i> <i>Helleborus niger,</i> <i>Costus sp.,</i> <i>Lagoecia cuminoides,</i> <i>Glaucium flavum,</i> <i>Valeriana dioscorides,</i> <i>Agrimonia eupatoria,</i> wolf liver, honey	Analgesic and efficient in sensory impairment	Volume 4/p. 448
Ethanasia al-Soghra	Electuary	<i>Liquidambar orientalis,</i> <i>Crocus sativus,</i> <i>Costus sp.,</i> <i>Valeriana dioscorides,</i> <i>Papaver somniferum,</i> <i>Cinnamomum iners,</i> <i>Agrimonia eupatoria,</i> <i>Iris spp.,</i> honey	Analgesic and efficient in sensory impairment	Volume 4/p. 449
Belazori	Electuary	<i>Cuscuta epithymum,</i> <i>Iris florentina,</i> <i>Rheum palmatum,</i> <i>Crocus sativus,</i> <i>Zingiber officinale,</i> <i>Cinnamomum iners,</i> <i>Valeriana dioscorides,</i> <i>Cinnamomum tamala,</i> <i>Artemisia herba-alba,</i> <i>Aloe barbadensis,</i> <i>Polyporus officinalis,</i> <i>Areca catechu,</i> <i>Eugenia caryophyllata,</i> <i>Andropogon schoenanthus,</i> <i>Moringa Arabica,</i> <i>Moringa pterygosperma,</i> honey	Efficient in paresis and nerves diseases	Volume 4/p. 446

Table 3 – (Continued)

Name of compound medicine	Dosage form	Ingredients	Chief virtue of the compound based on original text*	Volume/pages of source (Canon)
Ayarej-e loghafia	Electuary	<i>Pistacia lentiscus, Aloe barbadensis, Cinnamomum zeylanicum, Valeriana dioscoridis, Asarum sp., Commiphora opobalsamum, Crocus sativus, Cinnamomum iners, honey</i>	Efficient in nerve diseases and organ paresis	Volume 4/p. 462
Habb al-Estamhighoon	Tablet	<i>Terminalia chebula, Artemisia absinthium, Polyporus officinalis, Convolvulus scammonia, Asarum sp., Pimpinella anisum, Apium graveolens, Ipomoea turpethum, Ayarej-e Fighara (a Persian medicine compound), Eugenia caryophyllata</i>	Purgative for dense materials from nerves	Volume 4/p. 534
Habb al-Sheitaraj	Tablet	<i>Ferula persica, Dorema ammoniacum, Commiphora mukul, Opopanax chironium, Cuscuta epithymum, Polyporus officinalis, Castoreum, Crocus sativus, Citrullus colocynthis, Centaurium minus, Aloe barbadensis, Aristolochia longa, Piper longum, Zingiber officinale, Carum copticum, Apium graveolens, Pimpinella anisum, Commiphora myrrha, Euphorbia sp., Lepidium latifolium</i>	Purgative for dense materials from nerves	Volume 4/p. 532
Ayarej-e Jalinus	Electuary	<i>Ferula persica, Dorema ammoniacum, Commiphora mukul, Opopanax chironium, Cuscuta epithymum, Polyporus officinalis, Castoreum, Crocus sativus, Citrullus colocynthis, Helleborus niger, Hypericum perforatum, Polypodium vulgare, Marrubium vulgare, Cinnamomum iners, Commiphora myrrha, Aristolochia longa, Piper nigrum, Cinnamomum zeylanicum, Athamanta Macedonia, Carum petroselinum, honey</i>	Purgative for dense materials from nerves	Volume 4/p. 467

* This column is based on terminologies from Persian medicine.

occur first, and wrist drop, thenar atrophy, and motor damage can also occur later.^{17,21}

According to Avicenna, one of the causes of *khadar* is nerve compression syndrome (entrapment neuropathy), which is similar to the pathophysiology of compressive neuropathy in CTS. The interesting thing is that Avicenna also noted other nonphysical reasons for sensory neuropathy. Avicenna believed that disturbed balance among the four body humors and alteration in the nerve temperament that prevents the transmission of nerve impulses are other causes of sensory

neuropathy. These ideas could be potentially accompanied by a new approach for the prevention and treatment of the disease.

4.3. Therapeutic approaches

As mentioned earlier, humoral and temperament approach of Persian medicine to sensory mononeuropathy leads to the presentation of preventive therapeutic ways, which are different from conventional medicine. According to the basic theory

Table 4 – CTS in Persian medicine (Avicenna's words) at a glance

Field	Persian medicine concept
Name	Neuralgia, paresthesia
Etiology	1. Nerve compression (entrapment neuropathy); 2. Nonphysical reasons: Disturbed balance among the four body humors; 3. Alteration in the nerve's temperament that prevents the transmission of nerve impulses; 4. Some other etiologies such as nutrition, mental condition, sleep, weather condition, body movements, and proper disposal of body waste.
Symptoms	Pain, paresthesia, hypoesthesia, tingling, and numbness
Treatments	1. Lifestyle modifications 2. Pharmacotherapy (oral and topical herbal remedies)

of humorism (PM theory), accumulation of thick humors and imbalance in body temperament and humors can cause diseases and disorders. On the basis of this theory, from Avicenna's viewpoints, the prevention and treatment of median nerve mononeuropathy (such as CTS) consist of the following measures:

4.3.1. Lifestyle modification

Avicenna explained in detail the main lifestyle factors influencing bodily health. The second section of the first book of Canon of Medicine principally deals with six essential factors, "Asbab-e-Settah-e-Zaruriah," as a preventive/therapeutic strategy. He stated that any abnormality in these factors could primarily cause distemperament and then could make the body susceptible to various kinds of diseases, including mononeuropathy.²⁶ These factors are summarized in Table 1.

4.3.2. Pharmacotherapy

The principal strategy that Avicenna introduced in the treatment of nerve disease, including mononeuropathies, is the correction of nerve temperament (*Mizaj*) and purgation from cold natured (*mavad-al-barede*) substances. He also recommended nonpharmacological interventions for the next step in some special situations. Numerous oral or topical herbal remedies have been offered by Avicenna in the Canon of Medicine to treat sensory neuropathic pain. Tables 2 and 3 show some medical plants and compound medicines mentioned in the Canon of Medicine for sensory neuropathy, respectively.

5. Discussion

Although carpal tunnel syndrome is a new term in medicine and did not exist in the medieval period, it seems that Avicenna was familiar with this kind of disease and explained nerve diseases in detail in the Canon of Medicine (Table 4). Results show that the pathophysiology of sensory mononeuropathy such as CTS had been explained by him. Avicenna believed some other etiologies to be responsible for CTS such as nutrition, mental condition, sleep, weather condition, body movements, proper disposal of body waste, and finally balances between temperament and humors. He presented many lifestyle modifications for these patients. Current

studies indicate that there are some nonpharmacological solutions such as exercise, rehabilitation, and yoga for CTS patients with mild-to-moderate symptoms.^{72–74} Furthermore, nutritional shortages such as vitamin B6 deficiency are considered to be responsible for promoting CTS.⁷⁵

In intervention, current findings support the usage of remedies with antioxidant, anti-inflammatory, analgesic and neuroprotective effects to manage CTS, at least in mild-to-moderate phases.^{74,76} Therefore, there is acceptable hypothesis for most of Avicenna's prescriptions because of such effects. On the basis of such theories, currently some clinical trials were published showing the efficacy of some remedies from Persian medicine for CTS. For example, linseed oil improves the severity of symptoms and functional scores, as well as median nerve conduction velocity, in mild or moderate CTS.⁶⁶ In another study, Setayesh et al showed that topical application of flax seed oil gel, twice a day for three weeks, was more effective than hand splint for reduction of symptoms and functional improvement of patients with mild-to-moderate CTS.⁷⁷ Various herbal products with different known mechanisms such as analgesic, antioxidant, and anti-inflammatory that increase organ perfusion have also been recommended. Traditional chamomile oil is another example that has efficacy on both mild and moderate,⁷⁸ as well as severe,⁵³ CTS. Therefore, besides the historical importance of such a study for showing human knowledge on carpal tunnel syndrome in about the past 1000 years, this study also helps to hypothesize and find natural remedies as complementary medications for CTS looking at history through the ages.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgment

This study was a part of the PhD thesis (Registered Number: 93-112) by Dr. Mohammad Setayesh, who was supported by the Tehran University of Medical Sciences.

References

1. MacDermid JC, Doherty T. Clinical and electrodiagnostic testing of carpal tunnel syndrome: a narrative review. *J Orthop Sports Phys Ther* 2004;34:565–88.
2. Atroshi I, Gummesson C, Johnsson R, Ornstein E, Ranstam J, Rosén I. Prevalence of carpal tunnel syndrome in a general population. *JAMA* 2009;282:153–8.
3. Bland JDP. Carpal tunnel syndrome. *BMJ* 2007;335:343–6.
4. Dale AM, Harris-Adamson C, Rempel D, Gerr F, Hegmann K, Silverstein B, et al. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. *Scand J Work Environ Health* 2013;39:495–505.
5. De Krom MCTFM, Knipschild PG, Kester ADM, Thijs CT, Boekkooi PF, Spaans F. Carpal tunnel syndrome: prevalence in the general population. *J Clin Epidemiol* 1992;45:373–6.
6. Ibrahim I, Khan W, Goddard N, Smitham P. Carpal tunnel syndrome: a review of the recent literature. *Open Orthop J* 2012;6:69–76.
7. Lewis C, Mauffrey C, Newman S, Lambert A, Hull P. Current concepts in carpal tunnel syndrome: a review of the literature. *Eur J Orthop Surg Traumatol* 2010;20:445–52.
8. Scalco RS, Pietroski F, Celli LFS, Gomes I, Becker J. Seasonal variation in prevalence of carpal tunnel syndrome. *Muscle Nerve* 2013;47:925–7.
9. Palmer KT. Carpal tunnel syndrome: the role of occupational factors. *Best Pract Res Clin Rheumatol* 2011;25:15–29.
10. Barcenilla A, March LM, Chen JS, Sambrook PN. Carpal tunnel syndrome and its relationship to occupation: a meta-analysis. *Rheumatology (Oxford)* 2012;51:250–61.
11. Zyluk A. Is carpal tunnel syndrome an occupational disease? A review. *Pol Orthop Traumatol* 2013;78:121–6.
12. Evanoff B, Dale AM, Deych E, Ryan D, Franzblau A. Risk factors for incident carpal tunnel syndrome: results of a prospective cohort study of newly-hired workers. *Work* 2012;41:4450–2.
13. Foley M, Silverstein B, Polissar N. The economic burden of carpal tunnel syndrome: long-term earnings of CTS claimants in Washington State. *Am J Ind Med* 2007;50:155–72.
14. Prime MS, Palmer J, Khan WS, Goddard NJ. Is there light at the end of the tunnel? Controversies in the diagnosis and management of carpal tunnel syndrome. *Hand (N Y)* 2010;5:354–60.
15. Karne SS, Bhalerao NS. Carpal tunnel syndrome in hypothyroidism. *J Clin Diagn Res* 2016;10:36–8.
16. Shiri R. Hypothyroidism and carpal tunnel syndrome: a meta-analysis. *Muscle Nerve* 2014;50:879–83.
17. Aroori S, Spence RA. Carpal tunnel syndrome. *Ulster Med J* 2008;77:6–17.
18. Uchiyama S, Itsubo T, Nakamura K, Kato H, Yasutomi T, Momose T. Current concepts of carpal tunnel syndrome: pathophysiology, treatment, and evaluation. *J Orthop Sci* 2010;15:1–13.
19. Zyluk A. Carpal tunnel syndrome in pregnancy: a review. *Pol Orthop Traumatol* 2013;78:223–7.
20. Huisstede BM, Hoogvliet P, Randsdorp MS, Glerum S, van Middelkoop M, Koes BW. Carpal tunnel syndrome. Part I: effectiveness of nonsurgical treatments – a systematic review. *Arch Phys Med Rehabil* 2010;91:981–1004.
21. Padua L, Coraci D, Erra C, Pazzaglia C, Paolasso I, Loret C, et al. Carpal tunnel syndrome: clinical features, diagnosis, and management. *Lancet Neurol* 2016;15:1273–84.
22. World Health Organization. WHO traditional medicine strategy 2014–2023; 2014. http://www.who.int/medicines/publications/traditional/trm_strategy14.23/en/.
23. Balouchi A, Rahnama M, Hastings-Tolsma M, Shoja MM, Bolaydehyi E. Knowledge, attitude and use of complementary and integrative health strategies: a preliminary survey of Iranian nurses. *J Integr Med* 2016;14:121–7.
24. Flaherty G, Fitzgibbon J, Cantillon P. Attitudes of medical students toward the practice and teaching of integrative medicine. *J Integr Med* 2015;13:412–5.
25. Zargaran A, Zarshenas MM, Karimi A, Yarmohammadi H, Borhani-Haghghi A. Management of stroke as described by Ibn Sina (Avicenna) in the Canon of Medicine. *Int J Cardiol* 2013;169:233–7.
26. Choopani R, Emtiazy M. The concept of lifestyle factors, based on the teaching of Avicenna (Ibn Sina). *Int J Prev Med* 2015;6:30–7.
27. Jackson WA. A short guide to humoral medicine. *Trends Pharmacol Sci* 2001;22:487–9.
28. Zargaran A, Mehdizadeh A, Zarshenas MM, Mohagheghzadeh A. Avicenna (980–1037 AD). *J Neurol* 2012;259:389–90.
29. Zargaran A, Borhani-Haghghi A, Faridi P, Daneshamouz S, Mohagheghzadeh A. A review on the management of migraine in the Avicenna's Canon of Medicine. *Neurol Sci* 2016;37:471–8.
30. Pearce JM, John Fothergill: a biographical sketch and his contributions to neurology. *J Hist Neurosci* 2013;22:261–76.
31. Boskovski MT, Thomson JG. Acroparesthesia and carpal tunnel syndrome: a historical perspective. *J Hand Surg Am* 2014;39:1813–21.
32. Heydari M, Shams M, Hashempur MH, Dalfardi B, Borhani-Haghghi A. The origin of the concept of neuropathic pain in Early Medieval Persia (9th–12th century CE). *Acta Med Hist Adriat* 2015;13(Suppl 1):9–22.
33. Shoja MM, Tubbs RS, Loukas M, Khalili M, Alakbarli F, Cohen-Gadol AA. Vasovagal syncope in the Canon of Avicenna: the first mention of carotid artery hypersensitivity. *Int J Cardiol* 2009;134:297–301.
34. Abokrysha N. Ibn Sina (Avicenna) on pathogenesis of migraine compared with the recent theories. *Headache* 2009;49:923–7.
35. Resende LA, Weber S. Peripheral facial palsy in the past: contributions from Avicenna, Nicolaus Friedreich and Charles Bell. *Arq Neuropsiquiatr* 2008;66:765–9.
36. Zargaran A, Zarshenas MM, Mehdizadeh A, Mohagheghzadeh A. Management of tremor in medieval Persia. *J Hist Neurosci* 2013;22:53–61.
37. Avicenna H. Al-Qanun fi-al-Tib [The Canon of Medicine]. Beirut, Lebanon: Dar-Ehya-al-Torath-al-Arabi; 2005 [In Arabic].
38. Rajamurugan R, Selvaganabathy N, Kumaravel S, Ramamurthy C, Sujatha V, Thirunavukkarasu C. Polyphenol contents and antioxidant activity of Brassica nigra (L.) Koch. leaf extract. *Nat Prod Res* 2012;26:2208–10.
39. Selim S, Al Jaouni S. Anti-inflammatory, antioxidant and antiangiogenic activities of diosgenin isolated from traditional medicinal plant, Costus speciosus (Koen ex. Retz.) Sm. *Nat Prod Res* 2016;30:1830–3.
40. Chen L, Liu J, Zhang Y, Dai B, An Y, Yu LL. Structural, thermal, and anti-inflammatory properties of a novel pectic polysaccharide from alfalfa (*Medicago sativa* L.) stem. *J Agric Food Chem* 2015;63:3219–28.
41. Sadeghi L, Tanwir F, Yousefi Babadi V. Antioxidant effects of alfalfa can improve iron oxide nanoparticle damage: in vivo and in vitro studies. *Regul Toxicol Pharmacol* 2016;81:39–46.
42. Ratheesh M, Shyni GL, Helen A. Methanolic extract of Ruta graveolens L. inhibits inflammation and oxidative stress in adjuvant induced model of arthritis in rats. *Inflammopharmacology* 2009;17:100–5.

43. Ivanova D, Vankova D, Nashar M. *Agrimonia eupatoria* tea consumption in relation to markers of inflammation, oxidative status and lipid metabolism in healthy subjects. *Arch Physiol Biochem* 2013;119:32–7.
44. Saito N, Toki K, Moriyama H, Shigihara A, Honda T. Acylated anthocyanins from the blue-violet flowers of *Anemone coronaria*. *Phytochemistry* 2002;60:365–73.
45. Nesa L, Munira S, Mollika S, Islam M, Choin H, Chouduri AU, et al. Evaluation of analgesic, anti-inflammatory and CNS depressant activities of methanolic extract of *Lawsonia inermis* barks in mice. *Avicenna J Phytomed* 2014;4:287–96.
46. Reddy S, Rao G, Shetty B, Hn G. Effects of *Acorus calamus* rhizome extract on the neuromodulatory system in restraint stress male rats. *Turk Neurosurg* 2015;25:425–31.
47. Alania M, Shalashvili K, Sagareishvili T, Kavtaradze N, Sutiashvili M. Study of antioxidant activity of phenolic compounds from some species of Georgian flora. *Georgian Med News* 2013;222:69–72.
48. Sarahroodi S, Jafari-Najafi R, Nasri S, Rohampour K, Maleki-Jamshid A, Esmaeli S. Effects of *Nepeta menthoides* aqueous extract on retention and retrieval of memory in mice. *Pak J Biol Sci* 2012;15:1085–9.
49. Yun HM, Ban JO, Park KR, Lee CK, Jeong HS, Han SB, et al. Potential therapeutic effects of functionally active compounds isolated from garlic. *Pharmacol Ther* 2014;142:183–95.
50. Atkin M, Laight D, Cummings MH. The effects of garlic extract upon endothelial function, vascular inflammation, oxidative stress and insulin resistance in adults with type 2 diabetes at high cardiovascular risk. A pilot double blind randomized placebo controlled trial. *J Diabetes Complications* 2016;30:723–7.
51. Fitsiou E, Mitropoulou G, Spyridopoulou K, Tiptiri-Kourpeti A, Vamvakias M, Bardouki H, et al. Phytochemical profile and evaluation of the biological activities of essential oils derived from the Greek aromatic plant species *Ocimum basilicum*, *Mentha spicata*, *Pimpinella anisum* and *Fortunella margarita*. *Molecules* (Basel, Switzerland) 2016;21:1069.
52. Wierzchowska-Renke K, Tokarz H, Skorkowska M. Studies of *Asarum europaeum* L. II. Preliminary studies of the content of volatile oil and L-ascorbic acid in Herba Asari cum radicibus obtained at the Gdansk coastal region. *Acta Pol Pharm* 1970;27:63–9.
53. Hashempur MH, Lari ZN, Ghoreishi PS, Daneshfard B, Ghasemi MS, Homayouni K, et al. A pilot randomized double-blind placebo-controlled trial on topical chamomile (*Matricaria chamomilla* L.) oil for severe carpal tunnel syndrome. *Complement Ther Clin Pract* 2015;21:223–8.
54. Ahmad B, Khan H, Bashir S, Nisar M, Hassan M. Inhibition activities of *Colchicum luteum* baker on lipoxygenase and other enzymes. *J Enzyme Inhib Med Chem* 2006;21:449–52.
55. Yasukawa K, Matsubara H, Sano Y. Inhibitory effect of the flowers of artichoke (*Cynara cardunculus*) on TPA-induced inflammation and tumor promotion in two-stage carcinogenesis in mouse skin. *J Nat Med* 2010;64:388–91.
56. Verma SK, Jain V, Katewa SS. Blood pressure lowering, fibrinolysis enhancing and antioxidant activities of cardamom (*Elettaria cardamomum*). *Indian J Biochem Biophys* 2009;46:503–6.
57. Ismail H, Mirza B. Evaluation of analgesic, anti-inflammatory, anti-depressant and anti-coagulant properties of *Lactuca sativa* (CV. Grand Rapids) plant tissues and cell suspension in rats. *BMC Complement Altern Med* 2015;15:199.
58. Bouterfa K, Mehdadi Z, Elaoui MM, Latreche A, Benchiha W. Antioxidant activity and total phenolic and flavonoids content variations of leaves extracts of white Horehound (*Marrubium vulgare* Linne) from three geographical origins. *Ann Pharm Fr* 2016;74:453–62.
59. Chan EW, Lye PY, Wong SK. Phytochemistry, pharmacology, and clinical trials of *Morus alba*. *Chin J Nat Med* 2016;14:17–30.
60. Fatrcova-Sramkova K, Nozkoval J, Kacaniova M, Mariassyova M, Rovna K, Stricik M. Antioxidant and antimicrobial properties of monofloral bee pollen. *J Environ Sci Health B* 2013;48:133–8.
61. Mahboubi M. *Rosa damascena* as holy ancient herb with novel applications. *J Tradit Complement Med* 2016;6:10–6.
62. Senol FS, Orhan IE, Ustun O. In vitro cholinesterase inhibitory and antioxidant effect of selected coniferous tree species. *Asian Pac J Trop Med* 2015;8:269–75.
63. Gupta SK, Kumar B, Nag TC, Srinivasan BP, Srivastava S, Gaur S, et al. Effects of *Trigonella foenum-graecum* (L.) on retinal oxidative stress, and proinflammatory and angiogenic molecular biomarkers in streptozotocin-induced diabetic rats. *Mol Cell Biochem* 2014;388:1–9.
64. Loued S, Berrougi H, Componova P, Ikhlaf S, Helal O, Khalil A. Extra-virgin olive oil consumption reduces the age-related decrease in HDL and paraoxonase 1 anti-inflammatory activities. *Br J Nutr* 2013;110:1272–84.
65. Venturini D, Simao AN, Urbano MR, Dichi I. Effects of extra virgin olive oil and fish oil on lipid profile and oxidative stress in patients with metabolic syndrome. *Nutrition* 2015;31:834–40.
66. Hashempur MH, Homayouni K, Ashraf A, Salehi A, Taghizadeh M, Heydari M. Effect of *Linum usitatissimum* L. (linseed) oil on mild and moderate carpal tunnel syndrome: a randomized, double-blind, placebo-controlled clinical trial. *Daru* 2014;22:43–52.
67. Heydari M, Homayouni K, Hashempur MH, Shams M. Topical *Citrullus colocynthis* (bitter apple) extract oil in painful diabetic neuropathy: a double-blind randomized placebo-controlled clinical trial. *J Diabetes* 2016;8:246–52.
68. Gebhardt R. Antioxidative, antiproliferative and biochemical effects in HepG2 cells of a homeopathic remedy and its constituent plant tinctures tested separately or in combination. *Arzneimittelforschung* 2003;53:823–30.
69. Ziglioli F, Frattini A, Maestroni U, Dinale F, Ciufidea M, Cortellini P. Vanilloid-mediated apoptosis in prostate cancer cells through a TRPV-1 dependent and a TRPV-1-independent mechanism. *Acta Biomed* 2009;80:13–20.
70. Noroozi S, Mosaffa F, Soltani F, Iranshahi M, Karimi G, Malekaneh M, et al. Antigenotoxic effects of the disulfide compound persicasulfide A (PSA) on rat lymphocytes exposed to oxidative stress. *Planta Med* 2009;75:32–6.
71. Adhami HR, Lutz J, Kahlig H, Zehl M, Krenn L. Compounds from gum ammoniacum with acetylcholinesterase inhibitory activity. *Sci Pharm* 2013;81:793–805.
72. Ballesteros-Pérez R, Plaza-Manzano G, Urraca-Gesto A, Romo-Romo F, de los Ángeles Atíñ-Arratibel M, Pecos-Martín D, et al. Effectiveness of nerve gliding exercises on carpal tunnel syndrome: a systematic review. *J Manipulat Physiol Ther* 2017;40:50–9.
73. Yoo W-g. Effect of the release exercise and exercise position in a patient with carpal tunnel syndrome. *J Phys Ther Sci* 2015;27:3345–6.
74. Wipperman J, Goerl K. Carpal tunnel syndrome: diagnosis and management. *Am Fam Physician* 2016;94:993–9.
75. Ellis J, Folkers K, Watanabe T, Kaji M, Saji S, Caldwell J, et al. Clinical results of a cross-over treatment with pyridoxine and placebo of the carpal tunnel syndrome. *Am J Clin Nutr* 1979;32:2040–6.
76. Ginanneschi F, Milani P, Filippou G, Mondelli M, Frediani B, Melcangi RC, et al. Evidences for antinociceptive effect of 17-alpha-hydroxyprogesterone caproate in carpal tunnel syndrome. *J Mol Neurosci* 2012;47:59–66.

-
77. Setayesh M, Sadeghifar AR, Nakhae N, Kamalinejad M, Rezaeizadeh H. A topical gel from flax seed oil compared with hand splint in carpal tunnel syndrome: a randomized clinical trial. *J Evid Based Complementary Altern Med* 2017;22:462–7.
 78. Hashempur MH, Ghasemi MS, Daneshfard B, Ghoreishi PS, Lari ZN, Homayouni K, et al. Efficacy of topical chamomile oil for mild and moderate carpal tunnel syndrome: a randomized double-blind placebo-controlled clinical trial. *Complement Ther Clin Pract* 2017;26:61–7.