Review Article

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

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

\textsuperscript{a} Department of Persian Medicine, School of Persian Medicine, Kerman University of Medical Sciences, Kerman, Iran
\textsuperscript{b} Department of Traditional Pharmacy, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
\textsuperscript{c} Department of History of Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran
\textsuperscript{d} Department of Orthopedic Surgery, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
\textsuperscript{e} Traditional and Complementary Medicine Research Center (TCMRC), Department of Traditional Medicine, School of Medicine, Arak University of Medical Sciences, Arak, Iran
\textsuperscript{f} Department of Persian Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran

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\textbf{A B S T R A C T}

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

* 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).
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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%.\(^2,3\) CTS is more common in females, during middle age, and in winter.\(^4,5\) This disease is also more common among employed individuals\(^6\) and is noted to be associated significantly with certain professions.\(^7,8\) 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.\(^9\) CTS is usually idiopathic; however, other diseases such as hypothyroidism,\(^10\) diabetes, rheumatoid arthritis, chronic renal failure, acromegaly, amyloidosis, hemophilia, gout, fracture and trauma in the carpal tunnel region, high BMI, pregnancy, and mitochondrial diseases\(^11\) can accelerate its development.\(^12\)

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.\(^13\)\(^,\)\(^14\) 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.\(^15\) Many studies have been conducted about the disease, but there is no consensus regarding the better options both in diagnostic and therapeutic methods.\(^16\)\(^,\)\(^17\) After pointing out the challenges in diagnosing and treating this disease, new ways to prevent the disease have been recommended.\(^18\)

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.\(^19\) Moreover, healthcare workers are developing more positive attitudes toward T&CM.\(^20\)\(^,\)\(^21\) A serious reassessment of the traditional sources of medical information can be considered a postmodern approach to finding solutions to old unsolved problems.\(^22\)

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.\(^23\) 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.\(^24\) 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.\(^25\) 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.\(^26\)\(^,\)\(^27\)

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.\(^28\) 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.\(^29\) Neuropathy was used in indexed medical articles for the first time in 1924.\(^30\) However, it seems that CTS was known by medieval physicians by other names and terminologies. Nerve-originated pain (naja al-asab) was used as a term in a 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).\(^31\)

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.\(^32\) 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
the various fields of science such as philosophy, astronomy, and especially medicine. 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, pharmacopoeia, etc. The third volume of this book begins with neuroscience topics, including nerve diseases and its treatment approaches. Neurology is one of his favorite field of study. For example, he made pioneering discoveries in the field of vasovagal syncope, migraine headache, peripheral facial palsy, and tremor. He had also explained the management of stroke, 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.

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). Although generally what Avicenna described refers to general or focal functional disinterest of the patient, as well as changes in tissue and nerves passing through the tunnel, and not anatomic 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.” 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. He believed that the involvement of a branch of a single peripheral nerve (mononeuropathy) causes motor or sensory impairment within the same innervated organ.

In another general classification, Avicenna divided neuropathy into several distinct groups, namely sensory impairment [Khadar], paresis [Estehk], paralysis [Fale], tremors [Rasheh], facial paralysis [Laghe], and spasms and muscle stiffness [Tashzanno].

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
hypoaesthesia. 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 2 – Medicinal plants in the Canon of Medicine for sensory neuropathy](image)

| Scientific name | Family | English common name | Traditional Persian name | Part use | Root of administration | Pharmacological effect* /type of study |
|-----------------|--------|---------------------|--------------------------|----------|------------------------|---------------------------------------|
| Brassica nigra (L) K. Koch | Brassicaceae | Mustard | Khadel | Seed | Topical | AO, AG/in vitro^38 |
| Costus sp. | Costaceae | Costus | Ghost | Root | Topical (oil) | AO, AG/in vitro^39 |
| Trifolium aureum Pollich | Papaveraceae | Large trefoil | Khandaghoghi | Leaf and Seed | Topical (oil) | – |
| Medicago sativa L. | Leguminosae | Alfalfa | Ratbeh (ghat) | Aerial parts | Topical (oil) | AO, Al/in vitro and in vivo^40,41 |
| Scolopendrium vulgare Sm. | Aspleniaceae | Hart’s-tongue | Osgholahgandrion | Leaf | Oral | – |
| Ruta graveolens L. | Rutaceae | Common rue | Ghafeth | Leaf | Oral | AO, Al/in vivo^42 |
| Agrimony eupatoria L. | Rosaceae | Agrimony | Leaf | Aerial parts | Oral | AO, Al/in vivo^43 |
| Anemone coronaria L. | Ranunculaceae | Anemone | Goyle bood | Aerial parts | Oral and topical | AO, Al/in vitro^44 |
| L. | Inermis | L. | Hana | leaf | Oral and topical | AO, Al, AG/in vivo^45 |
| Acorus calamus L. | Acoraceae | Sweet flag | Vaj | Root | Oral and topical | AO, Al/in vivo^46 |
| Pinus sylvestris L. | Pinaceae | Pine | Senobar (kaaj) | Fruit | Oral | AO, Al/in vitro^47 |
| Nepeta menthoides Boiss. & Buhse | Lamiaceae | Lavender | Ostokhoddus | Aerial parts | Oral and topical | AO, Al/in vivo^48 |
| Allium sativum L. | Amaryllidaceae | Garlic | Sir (Soon) | Root | Oral and topical | AO, AG/Human study^49,50 |
| Pimpinella anisum L. | Apioideae | Anise | Asarum | Fruit | Oral and topical | AO, Al/in vitro^51 |
| Asarum europaeum L. | Aristolochiaceae | Asarabacca | Babon | Root-leaf | Oral and topical | AO, Al/in vitro^52 |
| Matricaria chamomilla L. | Asteraceae | Chamomile | Babon | Aerial parts | Oral and topical | AO, Al/Human study^53 |
| Colchicum autumnale L. | Colchicaceae | Meadow saffron | Suranjian | Flower-Seed | Oral and topical | Al/in vivo^44 |
| Cynara cardunculus L. | Asteraceae | Artichoke | Kangar | Aerial parts | Oral and topical | Al/in vivo^55 |
| Elettaria cardamomum (L.) Maton | Zingiberaceae | Cardamom | Ghagholeh (Heli) | Fruit | Oral and topical | Al/in vivo^56 |
| Lactuca sativa L. | Asteraceae | Lettuce | Kahoo | Seed | Oral and topical | AO, AI, AG/in vitro^57 |
| Marrubium vulgare L. | Moraceae | Marrubium | Toot sef | Leaf | Oral and topical | AO, Al/in vitro - in vivo^49 |
| L. | Morus alba L. | White mulberry | Toot sef | Aerial parts/Root | Oral and topical | AO, Al, AG/in vitro^58 |
| Papaver somniferum L. | Papaveraceae | Opium poppy | Khshhhash | Flower | Oral and topical | AO, Al/in vitro^60 |
| Rosa Damascena Mill. | Rosaceae | Rose | Vard Ahmar | Flower | Oral and topical | AO, Al, AG/in vitro and in vivo^41 |
| Taxus baccate L. | Taxaceae | Yew tree | Sorkhdaar | Aerial parts | Oral and topical | AO, Al/in vitro^62 |
| Trigonella foenum graecum L. | Fabaceae | Fenugreek | Shahnbalileh | Seed | Oral and topical | AO, Al/in vivo^63 |
| Olea europea L. | Oleaceae | Olive | Zeytoon | Fruit oil, leaf | Topical (oil) | AO, AI, NP/Human study^64,65 |
| Linum usitatissimum L. | Linaceae | Linseed | Katan | Seed | Topical (oil) | AO, AI, NP/Human study^66 |
| Citrullus colocynthis (L.) Schand. | Cucurbitaceae | Colocynthis | Hanzal | Fruit | Oral and topical | AO, AI, NP/Human study^67 |
| Veratrum album L. | Melanthiaceae | White hellebore | Kharbagh | Root | Oral | AO, Al/in vitro^68 |
| Euphorbia resinifera O. Berg. | Euphorbiaceae | Spurge | Farfon | Gum | Oral | Al/in vitro^69 |
| Ferula persica Willd. | Apiaceae | Ferula | Sabbinaj | Gum | Oral | AO/in vitro^70 |
| Dorema ammoniacum D. Don. | Apiaceae | Ammoniac Gum | Oshagh | Gum | Oral and topical | NP/in vitro^71 |

* AO: antioxidant; AI: anti-inflammatory; AG: analgesic; NP: neuroprotective.
| 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         | Commiphora myrrha, Cinnamomum iners, Teucrium montanum                        | Disentangling nerves obstructions                                                                                   | Volume 4/p. 541               |
| Dohn-e Hendi              | Oil         | Cydonia indica, Acorus calamus, Lepidium latfolium, Iris florentina, Inula heliönum, Zingiber zerumbet, Piper longum, Strychnos nux-vomica, Trichila emetica, Cupressus sempervirens, Populus, Costus sp., Foeniculum vulgare, Cedrus deodara, Doryoncum pardiæchæs | Analgesic for pain due to dense cold gas and humor in nerves                                                        | Volume 4/p. 544               |
| Dohn al-Zafran            | Oil         | Crocus sativus, Commiphora myrrha, Lagoecia cuminoides                        | Softening stiffness (inflammation) of nerves                                                                         | Volume 4/p. 545               |
| Dohn-e Ofarbion           | Oil         | Costus sp., Commiphora myrrha, Castoreum, Mentha pulegium, Anacyclus pyrethrum, Gypsophila struthium, Cheiranthus cheri, Iris florentia, Euphorbia sp. | Analgesic for cold nerves pain                                                                                      | Volume 4/p. 545               |
| Dohn-e Damamoon           | Oil         | Liquidambar orientalis, Pistacia lentiscus, Cinnamomum tamala, Valeriana dioesordises, Euphorbia sp., Cinnamomum zeylanicum, Apis mellifica, Moringa Arabica, Moringa pterygosperma, Commiphora opobalsamum, Piper nigrum | Preventing bad humors and materials to nerves and softening of the nerves                                           | Volume 4/p. 545               |
| Saoot                     | Snuff       | Citrullus colocynthis, Beta vulgaris, Medicago sativa, Nigella sativa, Peganum harmala | Efficient for cold pains and organ paresis; disentangling obstructions due to coldness and humidity in nerves         | Volume 4/p. 565               |
| Ethanasia al-Kobra        | Electuary   | Crocus sativus, Commiphora myrrha, Papaver somniniferum, Castoreum, Hyoscyamus albus, Helleborus niger, Costus sp., Lagoecia cuminoides, Glaucium flavum, Valeriana dioesordises, Agrimonia eupatoria, wolf liver, honey | Analgesic and efficient in sensory impairment                                                                     | Volume 4/p. 448               |
| Ethanasia al-Saghra       | Electuary   | Liquidambar orientalis, Crocus sativus, Costus sp., Valeriana dioesordises, Papaver somniniferum, Cinnamomum iners, Agrimonia eupatoria, Iris spp., honey | Analgesic and efficient in sensory impairment                                                                     | Volume 4/p. 449               |
| Belazori                  | Electuary   | Cuscuta epithymum, Iris florentina, Rheum palmatum, Crocus sativus, Zingiber officinale, Cinnamomum iners, Valeriana dioesordises, Cinnamomum tamala, Artemisia herba-alba, Aloe burbædensis, Polyporus officinalis, Areca catechu, Eugenia caryophyllata, Andropogan schoenanthus, Moringa Arabica, Moringa pterygosperma, 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  | Pistacia lentiscus, Aloe barbadensis, Cinnamomum zeylanicum, Valeriana dioecora, Asarum sp., Commiphora opobalsamum, Crocus sativus, Cinnamomum iners, honey | Efficient in nerve diseases and organ paresis | Volume 4/p. 462 |
| Habb al-Estamhighoon      | Tablet     | Terminalia chebula, Artemisia absinthium, Polyergus officinalis, Convolvulus scammonia, Asarum sp., Pimpinella anisum, Apium graveolens, Ipomoea turpethum, Ayarej-e Fighara (a Persian medicine compound), Eugenia caryophyllata | Purgative for dense materials from nerves | Volume 4/p. 534 |
| Habb al-Sheitaraj         | Tablet     | Ferula persica, Dorema ammoniacum, Commiphora mukul, Opopanax chirionium, Cuscuta epithymum, Polyergus officinalis, Cistus sativus, Citrus limon, Centaurium minus, Aloe barbadensis, Aristolochia longa, Piper longum, Zingiber officinalis, Carum copticum, Apium graveolens, Pimpinella anisum, Commiphora myrrha, Euphorbia sp., Lepidium latifolium | Purgative for dense materials from nerves | Volume 4/p. 532 |
| Ayarej-e Jalinos          | Electuary  | Ferula persica, Dorema ammoniacum, Commiphora mukul, Opopanax chirionium, Cuscuta epithymum, Polyergus officinalis, Castoreum, Crocus sativus, Citrus limon, Helichrysum sp., Hypericum perforatum, Polypodium vulgare, Marrubium vulgare, Cinnamomum iners, Commiphora myrrha, Aristolochia longa, Piper nigrum, Cinnamomum zeylanicum, Athamanta Macedonia, Carum petroselinum, honey | 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
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, “Asbāb-e-Settah-e-Zarurīh,” 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 (mawād-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.56 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,68 as well as severe,84 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.

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