



PERGAMON

Neuroscience and Biobehavioral Reviews 25 (2001) 455–461

NEUROSCIENCE AND
BIOBEHAVIORAL
REVIEWS

www.elsevier.com/locate/neubiorev

History of epilepsy in Medieval Iranian medicine

A. Gorji*, M. Khaleghi Ghadiri

Institut für Physiologie, Universität Münster, Robert-Koch-Strasse 27a, 48149 Münster, Germany

Received 1 April 2001; revised 18 June 2001; accepted 9 July 2001

Abstract

The history of epilepsy in Medieval Persian medicine is not well-known in the Western world. This article presents the clinical approaches according to which Medieval Iranian practitioners viewed epilepsy and dealt with its problems. The clinical viewpoints of epilepsy are collected from Medieval Persian scientific references. These describe clinical manifestations, basic mechanisms, etiologies, treatment and prognosis. Medieval Iranian practitioners provide detailed clinical information on epilepsy. They mention various forms and symptoms of epilepsy and its apparent causes and offer dietary and hygienic rules, as well as a long list of pharmacologic compounds for treating it. Their findings about epilepsy are very accurate and vivid and many of them are accepted even today. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Medieval literature; Persian history; Epilepsy; Traditional medicine; Seizures; Ancient history; Anticonvulsants; Basic mechanism

1. Introduction

The ancient Iranian medicine was combined by different medical traditions from Greece, Egypt, India and China for more than 4000 years and merged to form what became the nucleus and foundation of medical practice in the European countries in the 13th century. The Iranian academic centers like Jundishapur University (3rd century AD) were a breeding ground for the union among great scientists from different civilizations [1,2]. These centers successfully followed their predecessors' theories and greatly extended their scientific research through history. One of the main roles played by Medieval Iranian scholars in the scientific field was the conservation, consolidation, coordination and development of ideas and knowledge in ancient civilizations. Some Iranian *Hakim* (practitioners) such as Abu Bakr Muhammad ibn Zakariya Al-Râzi known to the West as Rhazes (b: 860 AD, Ray near modern Tehran—d: Ray, 940 AD) and Abu Ali Al-Hussain ibn Abdullah Ebn-e Sinâ better known as Avicenna (b: 980 AD, Afshana near Bukhara—d: Hamadan, 1037 AD) were not only responsible for accumulating all the existing information on medicine of the time, but adding to this knowledge by their own astute observations, experimentation and skills [3,4]. 'Qanoon fel teb of Avicenna' ('The Canon') and

'Kitab al-hawi of Râzi' ('Continens') were among the central texts in Western medical education from the 13th to the 18th centuries [5,6].

Many studies concerning the history of epilepsy have been performed [7–11]. In spite of these, the history of epilepsy in Iranian medicine has received scant attention from modern medical historians. The Iranian neuroscience history can be traced to the 3rd century BC, when the first cranial surgery was performed in the *Shahr-e-Sukhteh* (Burnt City) in south-eastern Iran. The archaeological studies on the skull of a 13-year-old girl suffering from hydrocephaly indicated that she had undergone cranial surgery to take a part of her skull bone and the girl lived for at least about 6 months after the surgery [12]. Epilepsy is an important issue in the field of traditional Persian 'neuroscience'. Although some studies have been performed on the history of Medieval Persian medicine [13–15], only Vanzan and Paladin reviewed the historical concepts of epilepsy in Persian culture [16]. Here we put special emphasis on the review of clinical aspects of epilepsy throughout Iranian medical history in the Middle Ages. Our main goal and intention in this study is: firstly, to isolate and analyze all of the clinical aspects of epilepsy in order to clarify the manner in which Medieval Iranian practitioners viewed and dealt with this problem. Secondly, to provide appropriate clinical data from centuries of experience in the field of epilepsy which may be helpful for testing their probable benefits for epileptic patients. In recent years, some experimental studies have indeed evaluated Medieval

* Corresponding author. Tel.: +49-251-8355564; fax: +49-251-8355551.

E-mail address: gorjial@uni-muenster.de (A. Gorji).

Iranian medical remedies using modern scientific methods. These studies raised the possibility of revival of traditional treatments on the basis of evidence-based medicine. Although the efficacy of some traditional antiepileptic drugs, as well as a common basic mechanism of action, was confirmed in different *in vivo* and *in vitro* epilepsy models [17–22], most ideas remain largely unexamined. Thus, it seems desirable that Western medicine takes some cognisance of the Medieval Persian medicine and its seemingly outdated beliefs in epilepsy.

2. Definition and clinical manifestations

In the texts of Medieval Iranian medicine, the terms denoting epilepsy or epileptic attacks are '*sare*' (falling sickness), '*omm-ol-sabyan*' (children epilepsy), and '*maraze-el-kaheni*' (diviners' illness) [23–25]. The descriptions of generalized seizures (grand mal) are very accurate in the 'Canon of Avicenna' and 'Continent of Râzi'. Râzi states: 'During the epileptic attacks, the patients fall to the ground, cry and froth at the mouth. In some patients bladder or bowel incontinence may occur' [24]. Ebn-e Sinâ defines the epilepsy as a manifestation which begins abruptly, although premonitory symptoms such as weakness, epigastric pressure or pain, depression, tongue paresthesia, spreading extremities paresthesia, sudden shock, incoherent speaking, nightmare and sadness usually start earlier [23]. Râzi adds headache, psychologic disorders, amnesia and gastrointestinal disturbances to above-mentioned premonitory symptoms. Avicenna defines an epileptic attack as '... the patient feels agitated and becomes unconscious, turning red and stares with eyes distortion ... Respiration is impaired and the patient becomes cyanotic'. The other described signs and symptoms in 'The Canon' are muscle contraction and spasm, dizziness, temporal palpitation, salivation, gnashing of teeth, vomiting and red eyes [23]. It is noted in 'The Canon' and 'Al-Hawi' that the epileptic attacks are recurrent with sudden onset and spontaneous recovery [23,24].

In diagnosis, Avicenna lays great emphasis on the pulse and on the inspection of the urine. According to him, each pulsation consists of four factors: expansion, pause, contraction, pause. There are several kinds of pulse determined by the extent of the expansion, the quality of the impact on the fingers of the observer, velocity, etc. He describes the pulse of epileptic patients as, 'irregular and protracted pulse with varied rate and strength'. He also reports that 'The urine of epileptic patients contains bubbles and glass-like materials ... first the urine is red and then becomes colorless' [23].

The characteristics of postictal state is also defined by Avicenna. It is described how the patients gradually regain consciousness, become depressive and complain of headache, muscle pain (especially in lumbar and sacral regions, neck and shoulder), hiccup, and tremor [23].

Another kind of epileptic attack which is explained in

Medieval Persian references is highly compatible with a complex partial seizure which becomes secondarily generalized as defined in the International Classification of Epileptic Seizures [26]. Avicenna points out that '... [the symptoms] begin with eye blinking and gnashing of teeth, follow by staring and neck spasm before changing to the general epilepsy'. In another case, this kind of epilepsy is defined as '... early shoulder or spinal column contractions before generalized epilepsy ...' [23].

The partial seizures are also described by Avicenna: '... the epilepsy restricts to discrete areas such as lids, tongue or lips... and the patients are conscious during the attacks' [23]. Râzi in the seventh section of his 'Al-Hawi' describes status epilepticus. He states that '... and in the event that epileptic attacks are continuous and repetitive, they may lead to death' [24]. We have not been able, however, to find any description of absence seizures under the category of epilepsy in Medieval Iranian medical references.

The complex relationship between migraine and epilepsy is observed by Râzi. In the headache section of his 'Al-Hawi', he explains a syndrome in which *bayzeh* (migraine headache) and *remed* (conjunctivitis) precede epileptic attacks [24].

3. Classification of epileptic seizures

Galen (about 175 AD) is possibly the first to systematize epilepsy [27]. According to Galen's theory of epilepsy, the brain can be affected either directly or indirectly from another part of the body. From this, he defines three types of epilepsy. The first type of epilepsy results from an idiopathic disease of the brain. In the second type, the brain's involvement is sympathetic, meaning that the brain is essentially healthy, but had become involved in a disease process originated outside it, typically in the cardia (the upper part of the stomach). The third type of epilepsy results from a sympathetic involvement of the brain originating in any other body part. Râzi repeats this classification in 'Al-Hawi' [24] while Avicenna classifies the epilepsy according to the different humors [23]. His classification is focused on the diagnostic approach on particular etiologies, selecting the appropriate therapy and providing some information regarding prognosis. He distinguishes four different types of epilepsy.

1. Phlegm type: this type is characterized by a long-term of unconsciousness, warm and sticky salivation, drowsiness, amnesia, paleness, anxiety and fear, increased bowel movements and melted glass-like substances in urine. Phlegm type epilepsy is divided into crude (cold) and salty subclasses based on the severity and duration of symptoms.
2. Black-bile type: this type is characterized by palpitation and dull chest pressure, obsession, unrealistic thinking, mouth dryness, leanness and false appetite. Black-bile

type epilepsy is divided into normal (dark) and burnt (sharp) subclasses. In the normal subclass, the patient is relaxed while in the other one he is agitated with insane behavior and sometimes fever.

3. Blood type: this type is characterized by red eyes, drowsiness, enlarged neck vein and cyanosis. It is pointed out that the effect of blood in this type is related to hyperemia or high pressure blood circulation (hypertension).
4. Yellow-bile type: this type is characterized by depression, short duration of attacks and yellow face.

It is noted that most patients are affected by phlegm and black-bile type while the yellow-bile type is very rare [23]. Another classification in 'The Canon' and 'Al-Hawi' distinguishes different forms of epilepsy depending upon the origin of the attacks. In this classification, epilepsy is divided into different kinds of liver type, stomach type, peritoneal (external layer) type, spleen type and uterus type. This classification reflects the varied symptomatology of epilepsy. In another classification the age of onset is used to define four types of seizures; infants, young children (<7 years), teenagers (around puberty) and adults. This classification provides some data regarding clinical courses and prognosis of epilepsy especially in febrile seizures [23,24].

4. Basic mechanisms

Al-Tabari (838–870 AD) is most famous for his world-renowned medical treatise 'Firdous al-Hikmat' ('Paradise of wisdom'). Divided into seven volumes, 'Firdous al-Hikmat' is the first ever medical encyclopaedia which incorporates all the branches of medical science in its folds. It synthesizes the Hippocratic and Galenic traditions of medicine with those of India and Persia. Al-Tabari discusses the head and brain diseases in details in section two of the 4th volume and classifies epilepsy among the brain diseases [25].

Al-Tabari like other Medieval Iranain practitioners specifies that the origin of epilepsy is the brain and the nerves. Galen locates epilepsy in the third and fourth ventricles [7,8], whereas Avicenna assigns the anterior ventricle to it, since the attacks initially affect the sense of hearing and sight as well as facial muscles. The injury of the anterior ventricle results in brain contraction and elicits the epileptic attacks. It is described that the injury is provoked by some pathologic processes such as unhealthy humor or vapour which relatively blocks the normal flow of the ventricle and the brain contracts in order to expel the harmful substances. The facial nerves follow this brain abnormal contraction. The origin of the abnormal movements of the other organs is referred to the transfer of brain contractions or to the direct effect of the pathologic processes. It is also stated that epilepsy may originate from the cortex or deeper brain structures [23–25].

Another explained mechanism of epilepsy is nerve spasms. Nerve spasms may originate in the brain or be

induced by nerve inflammations. The inflammatory substances are divided into intrinsic agents like phlegm humor and extrinsic factors such as scorpion venom. Avicenna notes that 'inflamed nerve fibers contract in a longitudinal sense and a concomitant expansion in a latitudinal sense'. Inflammations due to extrinsic factors can transfer to the brain and elicit seizures [23].

5. Etiology

The accurate observations in traditional Persian medicine emphasize the concept that many causes of seizures and epilepsy result from a dynamic interplay among endogenous factors, epileptogenic factors, and precipitating factors. It is suggested that the potential role of each needs to be considered in order to determine the appropriate management of a patient with epilepsy.

5.1. Endogenous factors

The main endogenous factor which is mentioned in Medieval Iranian medicine is high fever in children. Febrile seizure is described by Ebn-e Sinâ as 'an attack which usually occurs a short time after high fever ... in children under 7 years old'. It is noted that the children older than 7 years become epileptic only after a very high (burning) fever [23]. Pregnancy is another explained endogenous factor by both Avicenna and Râzi [23,24]. The definition of seizures in pregnant women is compatible with the attacks during eclampsia. Ebn-e Sinâ writes: 'sometimes epileptic attacks occur in the pregnant women. After delivery and rejecting the *hayy* (menstrual discharge) incompatible substances, the mothers become healthy' [23].

Instructions to the physician in dealing with patients are clearest in the 'Paradise of Wisdom'. This affirms that when dealing with a patient many details must be ascertained about him, among those is the medical history of his parents [25]. Familial occurrence of epilepsy is described [28].

5.2. Epileptogenic factors

A variety of factors are mentioned as an extremely high likelihood of resulting in a seizure disorder. Ebn-e Sinâ notes that hypoxia during delivery, is a potential cause of epilepsy. He concludes that absent nasal repelling of amniotic fluid after delivery induces epilepsy: 'the nasal discharges and also brain moisture must be expelled [by newborns] ... if not the child certainly is an epileptic patient' [23]. The Hippocratic surgeons mention the occurrence of convulsions as a sign of head trauma [7]. In line with that, trauma, but not explicitly head trauma, is mentioned as an epileptogenic factor. The practitioners have also recognized that the infectious disease lowered the seizure threshold. Avicenna reports that seizures may occur during the courses of some diseases such as diphtheria, pleuritis and visceral abscess [23]. Râzi believes

that parasites may cause epileptic attacks as he writes that ‘In my opinion, epilepsy can originate from intestinal worms. [In this case] symptoms are severe burning stomach discomfort before seizure attacks, salivation (slaver), and expulsion of the worm’ [24]. Avicenna mentions *Trichinella* as an example of these intestinal worms [23].

5.3. Precipitating factors

In Medieval Iranian medicine, it is well-known that the patients with epilepsy have seizures intermittently and many epileptics are completely normal for months or even years between seizures. They conclude that there are important provocative factors which elicit seizures in patients with epilepsy. These factors are also mentioned as the factors which are responsible for causing a single seizure in someone without epilepsy [23,24]. According to ‘The Canon’ and ‘Al-Hawi’, the precipitating factors are included due to intrinsic processes and to exogenous factors.

The intrinsic factors which provoke the seizure attacks comprise two groups: (1) psychological stress such as severe depression, overwhelming fright and anger; (2) physical stress such as sleep deprivation, visual stimuli (thunderstorm, flame, glittering or swift objects), auditory stimuli (shrill sounds), olfactory stimuli (sulfur or tar odour), fasting, postprandial exercise, excess of sexual intercourse, immobility and changes in climatic factors, including geographical position as well as environmental temperature and humidity.

The exogen provocative factors include exposure to toxic substances (Helleborus, myrrh, *Hyoscyamus niger*), certain medicaments such as some purgatives and emetics, Al-Kuhl (alcohol; wine), venomous snakebites, arthropod bites and stings (spider, scorpion), bee stings and dietary factors (celery, olive, coriander) [23,24,28].

5.4. Treatment

Based on the Medieval Iranian medicine, therapy for a patient with a seizure disorder is multimodal and includes treatment of underlying conditions that cause or contribute to the seizure, avoidance of precipitating factors and prescription of antiepileptic medicaments. Avicenna describes that the choice of therapy is often determined more by specific conditions of the patient. Indeed, epilepsy classification is an important element in designing the treatment plan in Medieval Persian medicine.

5.4.1. General recommendations

Ebn-e Sinâ and Râzi mention that patients must avoid swimming, cold or hot weather, staying in bath for too long, gluttony, postprandial exercise, swift motion, exhaustion, watching shiny objects, including the sun and moon, emotional excitement and excess of sexual intercourse. Migration to the temperate regions is recommended. Massage of the area from the chest to the lower organs (especially with narcissus, rue, sesame or castor oil and

melted tail), moderate physical exercise, sauna and washing with tepid water for their relaxing effects are advised. Plunging in warm mineral water or solutions containing soft compounds such as lily oil, acanthus or cnine is considered beneficial. Evacuation of the bowels is also advised (especially in phlegm type epilepsy). In the case of possible immediate epileptic attack, patients are advised to vomit (especially in stomach type of epilepsy). Dry-cupping of spinal column, neck, flanks and pectoral muscles is claimed to be useful. Avicenna mentions the success achieved by the ancient Greeks through inhalation of peony flower fumes. Suffumigation of a compound derived from black cumin, ammonia salt, pepper and ginger is also advised. It is reported that fasten the extremities before seizure attacks could cease or reduce their severity. Cautrize the fingers is also specified as a therapeutic method in some patients. It is ordered that during the seizure attacks, a soft spherical object should be laid between the teeth [23,24].

5.4.2. Diet therapy

The heart of Iranian practitioners’ therapeutics is found in the importance they placed on food and diet. Avicenna writes: ‘Most illnesses arise solely from long-continued errors of diet and regimen’ [23]. Diet therapy plays an important role in the management of epileptics. Avicenna advises that the main daily meal be divided into three parts, one-third for lunch and two-thirds for dinner, while Râzi recommends three separate equal meals. Practitioners recommend abstinence from olive, celery, coriander, leek, radish, turnip cabbage, broad bean, lentil, carrot, garlic, onion, dairy products especially milk and cheese, pepper, mustard, dried fruits, beef, mutton, and fish. Wine is to be avoided, and if imbibed, it should be in low quantity, be old and refined or mixed with water. Chicken, goat, fawn, birds such as dull-yellow partridge and sparrow, camel, rabbit, wild pig, dittany, pear, honey, nuts, pistachio, cashew, currant, rue, sweet fennel, pea-soup, fleawort, manna of hedysarum, cinnamon, alhaghi stalk and raw partridge liver are considered beneficial. Turtle blood and camel brain are recommended by Râzi as useful substances. Appropriate beverage include, oxymel mixed with origany, spearmint syrup, catkin syrup, honey mixed with water, aloes-wood (Orpine) decoction, rose-water, chicory syrup, *ma-o-shaeir* (beer without alcohol) and pumpkin juice. Consumption of diuretic compounds is believed to be very useful [23,24].

By analysing of the dietetic approaches used to treat epileptics, it seems that some patients are recommended to eat food with a high potassium concentration (such as meat, cashew, nuts and fig) whereas food containing low potassium (e.g. dairy products and apple) should be avoided. Thus, in this therapeutic strategy, potassium rich food is used to treat epilepsy. This method of treatment has stimulated the idea to study the effect of low extracellular potassium $[K^+]_0$ on the level of seizure susceptibility and to estimate the benefit of returning to normal $[K^+]_0$ in the

human neocortical brain slices. This study revealed that, in contrast to the well-established high potassium model of epilepsy, the opposite change in $[K^+]_0$ also induces epileptiform activity [17]. Furthermore, using the whole cell patch clamp method, reduction of $[K^+]_0$ also excites neuronal cells in rat hippocampal CA1 region [29]. These data represent a new model of epilepsy termed as ‘low potassium model of epilepsy’. This novel mechanism of epileptogenesis may provide an in vitro model for the development of new drugs against difficult-to-treat epilepsy as epileptiform burst discharges elicit by reduction of $[K^+]_0$ in guinea pig hippocampal slices are not affected by different anticonvulsants [30]. In addition, as returning $[K^+]_0$ to normal levels abolished the epileptiform discharges and thus representing an anticonvulsant effect, it was suggested that the method to increase $[K^+]_0$ might indeed be of benefit for some epileptics [17].

5.4.3. Electrical-shock therapy

Abu Al-faraj (b: 1226, Melitene, Armenia—d: 1286, Maragheh, Iran), a follower of Avicenna, is probably the first to use electricity to treat epilepsy and neurogenic diseases by using a certain type of fish called Torpedo or cramp fish, which was put alive in water and then connected to two straps of steel. When the patient held them, which he only do for a short time, he shivered and would throw them to the ground. In his book ‘Tarikh mukhtasar ad-dual’ (‘The Abridged History of the States’), Abu Al-faraj reports that after some days of this treatment the patient is cured from epilepsy [31].

5.4.4. Phlebotomy

Râzi recommends bleeding as an effective method for eliminating epilepsy when it originates from blood type humor (in patient with swollen jugular vein and bluish-puffy face) or excess of alcohol consumption [24,32]. Avicenna recommends a moderate bleeding in calf or wrist veins and suggests avoiding bleeding in carotid arteries in order to prevent brain infarction [23].

5.4.5. Anti-epileptic medicaments

An endless series of powders, theriacs, leeches, mixtures and tablets of various types, decoctions, ointments and plasters are prescribed. Physicians stress the importance of dose, and route of administration and define a schedule for drug administration. Antiepileptic drug therapy plan in Medieval Iranian medicine is individualized, given different single and combined drug-therapy with a dosing schedule for each of those. The well-known anticonvulsive drugs include *Lavandula stoechas*, beaver, mushroom mixed with almond oil, essential oil of *Eugenia caryophyllata* (clove oil), *Pimpinella anisum*, essential oil of *Valeriana officinalis*, balsam oil, *Foeniculum vulgare*, aloe-wood, *Levisticum Officinale*, *Melissa officinalis*, fruit of laurel, Taryagh (a drug composed of laurel seeds, aristolochia, myrrh and gentian), Chebulic myrobalan, seeds of *Foeniculum vulgare*, larch

agaric, *Boletus laris*, senna, wild rue, *Carum carvi*, squill bulb (sea-onion), *Anacyclus pyrethrum* (pellitory of spain), *Ipomoea turpethum* (turpeth), *Acorus calamus* and *Artemisia absinthium* [23,24,33]. ‘Al-Hawi’ recommends Viola oil for children epilepsy [24]. Avicenna and Râzi define that single or combined treatment with aforementioned anti-epileptic compounds in some patients ‘... completely abolished the seizure attacks’ while in the other epileptics ‘... reduced the frequency and severity of the attacks’ [23,24].

The anticonvulsant effects of some of the above-mentioned compounds were tested in different in vivo and in vitro models of epilepsy. *Lavandula stoechas* is a plant indigenous to the Arabic and Mediterranean Coasts as well as Asia Minor [34]. It has been used in the treatment of various diseases of the central nervous system, such as migraine and epilepsy, and as an antispasmodic and sedative remedy by lay-practitioners in the Middle East [18]. Several Attempts have been made to provide a scientific basis for the traditional use of *Lavandula stoechas*, and other compounds. In one study, the aqueous-methanolic extract of *Lavandula stoechas* reduced the severity and increased the latency of convulsions elicited by pentylenetetrazole in mice in vivo. This study suggested that the anticonvulsant effects of *Lavandula stoechas* may be related to its calcium channel blocking property [18]. *Pimpinella anisum* (Umbelliferae) is an herb indigenous to Iran, India, Turkey and many other warm regions in the world [35]. The aqueous extract of the collection of flowers, stems and leaves of *Pimpinella anisum* has been reported to delay the onset of picrotoxin-induced seizures in mice [19]. Another study investigated the anticonvulsant effects of an essential oil of the fruits of *Pimpinella anisum* against seizures induced by maximal electroshock or pentylenetetrazole in mice. The substance, in a dose dependent manner, significantly suppressed maximal electroshock- or pentylenetetrazole-induced hind limb tonic extensions as well as mortality [20]. Chemical studies have demonstrated the presence of eugenol, anethole, methylchavicol, anisaldehyde and estragole as the main compounds of the fruit essential oil of *Pimpinella anisum* [20]. The anticonvulsant activity of *Pimpinella anisum* may be related to estragole and eugenol present in the essential oil of the plant as their anticonvulsant activity has been shown in animal models [36]. Eugenol also presents in *Anacyclus pyrethrum*, a plant which is prescribed as an antiepileptic by Medieval Persian practitioners [37].

Extracts of *Valeriana officinalis* have been used in folkloric medicine for their sedative, hypnotic, tranquillizer and anticonvulsant effects [21]. Data confirmed that extracts of *Valeriana officinalis* inhibited the uptake and stimulated the release of GABA by an interaction with both pre- and post-synaptic mechanism of GABAergic neurons [21]. Valerian extracts inhibited [3H]flunitrazepam binding and potentiated K^+ or veratridine-stimulated release of radioactivity from hippocampal slices preloaded with [3H]GABA

[38,39]. *Eugenia caryophyllata* (Myrtaceae) is a plant indigenous to the Molucca Islands but cultivated on the islands of Penang, Ambon, Pemba, Zanzibar, Sumatra, Madagascar and Mauritius and the West Indies [40]. The buds of this plant have been used as an antiepileptic remedy by traditional healers in the Middle East. To evaluate the probable anticonvulsant effect of *Eugenia caryophyllata*, the effect of an essential oil obtained from the buds of this plant (clove oil) on the seizures induced by maximal electroshock or pentylenetetrazole in mice was studied. Clove oil significantly suppressed tonic maximal electroshock-induced convulsions and increased the threshold of clonic seizures elicited by intravenous infusion of pentylenetetrazole [22]. Phytochemical analysis of clove oil has shown the presence of carvacol, eugenol, α -humulene and β -caryophyllene [41]. The efficacy of an inhalable drug containing carvacol in control of human seizures has been reported [42]. These animal experiments confirm the anticonvulsant potency of some of the compounds which are recommended by Medieval Iranian practitioners in epilepsy treatment. However, further studies are needed to unambiguously clarify the clinical usefulness, as well as the mechanisms of action, of these substances.

5.4.6. Prognosis

According to Avicenna, the prognosis in epilepsy is divided into three groups: mild (good), moderate and severe (poor). The mild degree is classified in case of seizure attacks with short duration and light postictal depression. The criteria for the severe degree epilepsy comprise dyspnea and severe anxiety before and during the attack and long-term depression after that. The moderate degree is applied to the situation between mild and severe degrees [21]. Seizures originating cortical areas and epilepsy in children (including febrile seizures) are also cited as the favourable states while epilepsy with subcortical origin, onset of epilepsy in patients older than 25 years, phlegm type epilepsy and seizures induced by chronic and very high fever are categorized as the poor (malign) criteria by Avicenna and Râzi [21,22]. Al-Tabri defines anemia as a dangerous factor in epileptics and includes children and women as the vulnerable groups [25]. Paralysis and melancholy are mentioned as complications of epilepsy by both Râzi and Ebn-e Sinâ [23,24]. Suffocation due to respiratory muscles spasm is claimed as the main reason for death during the epileptic attacks [23].

Acknowledgements

We thank H. Gorji, H. Toosi, F. Abrishamchian and F. Nawabian for help in the literature search.

References

- [1] Behrouz R, Ourmazdi M, Reza'i P. Iran—The cradle of science. 21st ed., Iran Almanac, 1993, p. 115–8.
- [2] Meyerhof M. Science and medicine. In: Arnold T, Guillaume A, editors. The legacy of islam, London: Oxford University Press, 1952. p. 314–5.
- [3] Elgood C. A medical history of Persia and the eastern caliphate from the earliest times to the year 1932 AD, 1932. London: Cambridge University Press, 1951. p. V.
- [4] Elgood C. A medical history of Persia and the eastern caliphate from the earliest times to the year 1932 AD, 1932. London: Cambridge University Press, 1951. p. 205–9.
- [5] Siraisi NG. Avicenna in Renaissance Italy: the Canon and medical teaching in Italian universities after 1500, Princeton: Princeton University Press, 1987. p. 77–124.
- [6] Osler W. The evolution of modern science, New Haven: Yale University Press, 1921. p. 243.
- [7] Temkin O. The falling sickness: a history of epilepsy from Greeks to the beginnings of modern neurology, 35. Baltimore: Johns Hopkins University Press, 1994. p. 35.
- [8] Temkin O. The falling sickness: a history of epilepsy from Greeks to the beginnings of modern neurology, Baltimore: Johns Hopkins University Press, 1994. p. 85–137.
- [9] World health organization report. Epilepsy: historical overview. WHOOMS. Fact sheet N 168. 1997.
- [10] Gross RA. A brief history of epilepsy and its therapy in the western hemisphere. *Epilepsy Res* 1992;12:65–74.
- [11] Soria ED, Fine EJ. The medical–moral account on epilepsy by Pedro de Horta: a historical review. *Epilepsia* 1995;36(7):736–9.
- [12] Sajjadi SM. First brain surgery in 4800 years ago in Iran. In: Iran News Agency [online]. Available at www.irna.com. Accessed January 2, 1999.
- [13] Siddiqui MZ. Studies in Arabic and Persian medical literature. Calcutta: Calcutta University Press, 1959.
- [14] Jacquart D, Mischeu F. La medecine arabe et l'occident medieval, Paris: Maisonneuve et Larose, 1990. p. 55–79.
- [15] Klein-Franke F. Vorlesungen über die Medizin im Islam, Wiesbaden: Franz Steiner Verlag GmbH, 1982. p. 32–85.
- [16] Vanzan A, Paladin F. Epilepsy and Persian culture. *Epilepsia* 1992;33:1057–64.
- [17] Gorji A, Köhling R, Straub H, Höhling JM, Madeja M. Lowering the extracellular potassium concentration elicits epileptic activity in neocortical tissue of epileptic patients. *Eur J Neurosci* 2001;13(3):639–40.
- [18] Gilani AH, Aziz N, Khan MA, et al. Ethnopharmacological evaluation of the anticonvulsant, sedative and antispasmodic activities of *Lavandula stoechas* L. *J Ethnopharmacol* 2000;71:161–7.
- [19] Abdul-ghani AS, El-Lati SG, Sacaan AI, Suleiman MS. Anticonvulsant effects of some Arab medicinal plants. *Int J Crude Drug Res* 1987;25:39–43.
- [20] Pourgholami MH, Majzoob S, Javadi M, Kamalinejad M, Fanaee GHR, Sayyah M. The fruit essential oil of *Pimpinella ansium* exerts anticonvulsant effects in mice. *J Ethnopharmacol* 1999;66:211–5.
- [21] Oritz JG, Nieves-Natal J, Chavez P. Effects of *Valeriana officinalis* extracts on [3H]flunitrazepam binding, synaptosomal [3H]GABA uptake, and hippocampal [3H]GABA release. *Neurochem Res* 1999;24:1372–8.
- [22] Pourgholami MH, Kamalinejad M, Javadi M, Majzoob S, Sayyah M. Evaluation of the anticonvulsant activity of the essential oil of *Eugenia caryophyllata* in male mice. *J Ethnopharmacol* 1999;64:167–71.
- [23] Avicenna A. *Ghanoon dar Teb*, Tehran: Soroosh Press, 1988. p. 144–86.
- [24] Abu bakr Mohamad ibn Zakariya Râzi. *Al-Hawi*. Tehran: Al-Hawi Pharma., 1990, p. 129–53.
- [25] Tabari AR. *Firdausu'l hekmat*. Berlin: Sonner Druckerei, 1928.
- [26] Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International league Against Epilepsy. *Epilepsia* 1981;22:489–501.

- [27] Masland RL. The classification of the epilepsies: a historical review. In: Vinken PJ, Bruyn GW, editors. *Handbook of clinical neurology*, New York: North-Holland & Elsevier, 1974. p. 1–29.
- [28] Khosravi SM, Khosravi AA. *Sina traditional medicine*, Tehran: Mohammad Press, 1994. p. 32–35.
- [29] Gorji A, Siep E, Möddel G, Speckmann E-J. Effects of low potassium concentrations on resting membrane potentials and action potentials in rat hippocampal CA1 neurons. *Pflüger Arch* 2001;441(6):R205.
- [30] Gorji A, Madeja M, Straub H, Köhling R, Speckmann E-J. Lowering of the potassium concentration induces epileptiform activity in the guinea pig hippocampal slices. *Brain Res* 2001;908:130–9.
- [31] Al-Ibri I. *Tarikh mukhtasar ad-dual li Ibn al-Ibri*, Beirut: Dar-al-mashrek, 1992. p. 131.
- [32] Shahri J. *The miracle of medicine and remedy*, Tehran: Tehran-Khazar Press, 1969. p. 62–64.
- [33] Saneie S. *Remedy recipe*, Tehran: Hafez-Novin Press, 1991. p. 133–9.
- [34] Nadkarni KM. *Indian materia medica*, Bombay: Popular Prakashan, 1982. p. 730.
- [35] Zargari A. *Medicinal plants*, Tehran: Tehran University, 1989. p. 502–7.
- [36] Dallmeier K, Carlini EA. Anesthetic, hypothermic, myorelaxant and anticonvulsant effects of synthetic eugenol derivatives and natural analogues. *Pharmacology* 1981;22:113–27.
- [37] Sukumaran K, Kuttan R. Inhibition of tobacco-induced mutagenesis by eugenol and plant extracts. *Mutat Res* 1995;343:25–30.
- [38] Cavadas C, Araujo I, Cotrim MD, Amaral T, Cunha AP, Macedo T, Ribeiro CF. In vitro study on the interaction of *Valeriana officinalis* L. extracts and their amino acids on GABAA receptor in rat brain. *Arzneimittelforschung* 1995;45(7):753–5.
- [39] Santos MS, Ferreira F, Cunha AP, Carvalho AP, Ribeiro CF, Macedo T. Synaptosomal GABA release as influenced by valerian root extract—involvement of the GABA carrier. *Arch Int Pharmacodyn Ther* 1994;327(2):220–31.
- [40] Tyler VE, Brady LR, Robberts JE. *Pharmacognosy*, Philadelphia: Lea and Febiger, 1988. p. 103–35.
- [41] Yu J, Hungju F. Studies on the essential oils of clove buds and clove leaves. *Zhong Caoyao* 1981;12:339–42.
- [42] Xi LY, Zheng WM, Zhen SM, Xian NS. Rapid arrest of seizures with an inhalation aerosol containing diazepam. *Epilepsia* 1994;35(2):356–8.