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Historical Article

Prevention of Rabies by Application of *Lytta vesicatoria* in Persian Medicine Texts in Islamic Civilization

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Abstract

Rabies is one of the most lethal diseases in human history. From the past, various drugs have been used to prevent the contraction of the disease when being bitten by a rabid animal. An insect called *Darārī*h (*Lytta vesicatoria*), although poisonous, has in some cases been medically used. Greeks and Romans have used venomousness of this insect to treat skin diseases, but it has not been used to prevent rabies. This is a summative qualitative content analysis that focused on Persian Medicine (PM) texts from 2th to 13th AH centuries. Literature was searched during centuries 4th to 13th AH, by using this key words: (Darārīh), Utta vesicatoria) and after extracting the data and analyzing them, the results were presented. In TPM texts, this insect was used to prevent rabies. This study has shown that the use of *darārīh* (*Lytta vesicatoria*) in the prevention of rabies has been one of the innovations of the practitioners of Islamic civilization. The innovation proves that scholars in the period of Islamic civilization were not merely consumers or custodians of Roman, Greek, Indian, and Iranian knowledge, but added to it while preserving that knowledge.

Keywords: Lytta vesicatoria; Rabies; Islamic civilization; Persian medicine

Introduction

Rabies, which is referred to in the texts of the Islamic period as *kalab* or $d\bar{a}'a al-kalab$ (*(الحاب)*, *su ʿār* (*(مُسعار*) or *ʿanza* (*مُنزَة*), has been one of the oldest and deadliest diseases in human history [1]. The disease occurs in animals such as dogs, wolves, foxes, bears, horses, mules, and sometimes elephants and cows, and the end result for the animal is nothing but death. Being bitten by an infected animal could transmit the disease to

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Copyright © 2021 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences.

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons. by NC humans. According to written sources in Iranian medicine, the symptoms of this disease are similar to the effects of insanity and melancholia, and the most important symptom of this disease in the advanced stages is hydrophobia.

The Greeks, followed by the Romans, called the disease lyssa and rabies because of the insanity that afflicted the patient [2,3]. In the Arab world and the Semitic tribes, the name of this disease (*Kalab*) is derived from the specific symptom of this disease. *Kalab* (in Arabic) means thirst and a patient with rabies suffers from severe thirst but unfortunately, due to the progressive dysphagia, and the excessive tendency to dryness and the appearance of hydrophobia he/she cannot drink water [4].

Today, nearly sixty thousand people die each year from rabies [5]. Due to its incidence, geographical distribution, high mortality, human and animal costs, this disease is one of the most important viral zoonosis that imposes high economic costs annually to different countries of the world, especially in Asia and Africa [6].

In Iran, this disease is endemic and in addition it is the most important zoonotic disease in the country [7]. According to a survey, almost all the provinces of the country are more or less polluted. The highest incidence of the disease is observed in the vicinity of Caspian Sea, northeastern and southwestern regions of the country [8].

To prevent and sometimes treat rabies, various drugs have long been common among tribes and nations. In Greek and Roman medical texts, Alyssum and river crabs, as well as grilled rabid dog liver, have been introduced as one of the most popular drugs for the prevention and treatment of rabies [9-11]. In the period of Islamic civilization, among the drugs announced in the prevention and treatment of rabies, name of an insect can be seen. An insect which its powdered body has been described as a drug with a surprising effect on rabies [12]. This insect and the medicine that was prepared from its body are also mentioned in the medical and pharmaceutical texts of Greece and Rome. The insect, in question, is called Darārīh (ذرارير) (Lytta vesicatoria) which the Greeks called cantharis [13]. And in Persian language, it has been known by various names in different regions [14]. Numerous medicinal uses for the insect have been defined in Greek and Roman medicine, including for the treatment of skin diseases, the removal of whiteness on the nails, in the treatment of scabies, as well as the cancerous swellings [13]. The medical application of this insect also had a relatively delicate process as follows: a number of these insects were placed in an earthenware container and the opening of the container covered with a clean cloth made of linen, and then the container was turned upside down and its mouth was placed on another container containing boiling vinegar. The steam of vinegar will suffocate the insect. The insects were then pulled into a string of linen and rubbed and consumed when needed [10,15]. Today, the effective drug extracted from this insect is called Cantharid, and it is mainly used in Invitro and Invivo trials for the treatment of skin diseases and cancer [16-18].

A study of medical and non-medical texts in the period of Islamic civilization on rabies gives researchers a very important and valuable point, and that is the new use of Lytta vesicatoria in the prevention and treatment of rabies. This application has not been recognized in any of the modern and contemporary medical texts and no attention has been paid to it. Perhaps due to the existence of preventive treatments with vaccines, the approach to it seems futile. However, the historical aspects of this discussion and even the possibility of conducting laboratory studies to prove the effectiveness of this drug in the prevention of rabies will be a good justification for a research in this field. Dr. Mirza 'Abd ul-Hussein Khan, known as the "Filsuf al Dawlah" physician of the Nāşir al-Dīn Shah period, in his book "The acquaintance with the toxins" refers to the application of Lytta vesicatoria in treating rabies by an Austrian physician [19].

Methods

This article is a summative qualitative content analysis that processed in seven classic steps:(20,21)

1. The research questions to be answered: "What is rabies disease in the Persian medicine texts, we don't find any disease that called as "Rabies"; To find the name of "Rabies" disease in the context of Persian medicine, we tried to collect all data's about rabies in the context of up to date modern texts; This information includes etiology, symptoms, signs, risk factor and treatment of rabies. And then we tried to find one disease have most overlap with rabies. As a result, rabies in Persian Medicine texts is known as "*kalab or dā'a al-kalab*"[1].

2. Selecting the sample to be analyzed: In this study, all of available medical texts of the Is-

Author	Title of the Book	Date Written	Subject	reference
فراهیدی /Farāhīdī Ḫ	كتاب العين /Kitāb ul ʿAyn	سده دوم /8 th century هجری	An Arabic Lexicon	[4]
بلاذری /Balā <u>d</u> urī A	انساب /Ansāb al [°] Ašrāf' انساب الاشراف	سدہ سوم /9 th century هجری	Biographies of the no- blemen	[22]
Al-Ğāḥiẓ A/ جاحظ	الحيوان /Al-Ḥayawān	سدہ سوم /9 th century هجری	Miscellaneous but gener- ally about animals	[23]
Razī M/ Rhazes/ Ra- sis/ محمد بن زكريا رازى	Al Ḥāvī fi al Ţibb	سدہ چھارم /10 th century ھجری	Medicine	[9]
`Ahwāzī A. على بن /Haly Abbas عباس اهوازى	complete book of the medical art (Kāmil al- Ṣināʿa al-Ṭibbīya or Royal Medicine)	سدہ چہارم /10 th century هجری	Medicine	[15]
ابوريحان /.Bīrūnī M بيروني	Al Şaydana	سدہ پنجم /11 th century هجری	Pharmacology	[11]
<i>Avicenna</i> <i>Ibn Sīnā H/</i> ابن سینا	Canon on Medicine (Al Qānūn fi al Ṭibb)	سده پنجم /'th century هجری	Medicine	[10]
Čurğānī SI./ سيد اسماعيل جرجاني	Dahīra hārazmšāhīi & Al ʿAġrāḍ al-Ṭibbīya wa al mabāhiṯ al ʿAlāīya	سدہ ششم /12 th century هجری	Medicine	[24]

Table 1: Historical books:

جواليقى /Čawālīqī M	شرح /Šarḥ ʾAdab il Kātib ادب الكاتب	سدہ ششم /12 th century هجری	A Literary book	[25]
ابن بيطار /Ibn Bayṭār	Tafsīr-u Kitāb discoridus	سدہ ھفتم /13 th century ھجری	Medicinal Herbs	[13]
/ـ <i>Ḥakīm Muʾmin M.</i> حكيم مومن	Tuḥfat al Muʾminīn	سده یازدهم /17 th century هجری	Traditional Medicine and Pharmacology	[14]

In the second step, the databases were searched by using key words of "rabies's etiology, prevention and treatment" in PubMed, PMC, Google Scholar and Scopus.

lamic civilization texts in this field were selected. These texts included manuscripts (the book itself or its electronic file) in different centuries from 11 to 20 A.D. we studied and searched historical books are in table 1.

Results

*Darārī*h and Its Application in Medicine of Islamic Civilization:

Darārīh (Lytta vesicatoria) in Arabic language is the name of a poisonous insect which was applied to make poison. Although this word has the plural form, but refers to a singular meaning. Its singular form has been said in different forms as follow: Durrāh, Durahraha, Darrūh and *Darīha*. The book of *Al-'Ain* compiled by Khalīl ibn Ahmad Farāhīdī (d. 170 AH) is the oldest Arabic source in which the word Darārīh (Lytta vesicatoria) is mentioned. This insect has been introduced in the entry of "Darh" as follows: "The insect is slightly larger than a fly, with colorful red, black, and yellow lines and spots on its body. It has two wings which flies with them. The toxicity of this insect must be reduced by mixing with other things [4].

 $Far\bar{a}h\bar{i}d\bar{i}$ wrote about the disease rabies and mentioned ways to treat it. He wrote:" it is said that to cure this disease a few number of *Lytta vesicatoria* should be dried in the shade, then crushed and sifted. This powder of *Lytta vesicatoria* must be mixed with lentils with a ratio of one to seven respectively. The mixture again should be mixed with pure wine and kept in a jar. This mixture must be prescribed for patients bitten by rabid animals. After taking the medicine, the patient should not sleep but should stand under the sunlight to sweat. This must be repeated several times in order to be healed by God's will" [25].

'Isa ibn Hakam of Damascus (living in 225 AH), known as Masih (Christ), has introduced the drug Lytta vesicatoria in his treatise Al-Kāfīiya to prevent the contraction of rabies. "Some Lytta vesicatoria must be removed of their head, wings and legs. Then the rest should be soaked in buttermilk and dried in the shade, then crushed and sifted with silk cloth. Mix one part of Lytta vesicatoria with two parts of peeled lentils and knead with oil and divide it into pills that weigh two *dāniq* (a weight unit) each. When taking it, take a pill with lukewarm water and stand in front of the sun of which one hour has passed from its rise. Wear thin clothes and run fast to get tired and sweat. When exhausted then warm animal fats or plant oil must be eaten. If he needs to urinate then must sit in warm water. The sign of healing is bloody urine! "[28].

Abul Hasan 'Alī ibn Raban Ţabarī (alive in 235 AH) was the third writer in the Islamic world after Khalīl ibn 'Ahmad and Ibn Hakam of Damascus to speak about the application of Lytta vesicatoria in the prevention of rabies. He wrote in more detail about the method of preventing rabies, almost the same way that Ibn Hakam wrote in Al-Kāfīiya treatise. Tabarī didn't identify his source but said: "My father used to say something strange about preventing rabies that had never been heard of before"[12]. These three reports are among the oldest references in Islamic civilization to the application of Lytta vesicatoria in the prevention of rabies. Rhazes (d. 313 AH) and Avicenna (d. 428 AH) have also repeated the contents of the three foretold authors in the use of Lytta vesicatoria in the prevention of hydrophobia. Razī has described Lytta vesicatoria as having a wonderful and good effect in preventing rabies, and Ibn Sīnā has called it beneficial [9,10]. *Bīrūnī* (d. 440 AH) has introduced Lytta vesicatoria in Saydana as follows: "it is a bee size animal, with yellow and red spots on his body. When a person grabs him, it constantly urinates. Like a bee, it has two wings to fly through. This insect is a poisonous killer. In order to mitigate the toxicity, the powdered insect will be mixed with lentils. The mixture will be applied to cure the patient bitten by a rabid dog. The mixture won't do any harm and will heal the wound" [11].

In the following centuries, physicians and writers of the Islamic period considered *Lytta vesicatoria* to be beneficial in preventing rabies or hydrophobia. In pre-Islamic Arabic literature, there is a story about a man named *Aswad ibn*

• *Auws* who learned the cure for rabies from $Na\check{g}a\check{s}\bar{\imath}$ (probably the ruler of Ethiopia). This method of treatment remained in his family, and one of those who survived the rabies with this treatment wrote a poem about it as follows:

If it weren't for *Ibn Muḥill's* medicine and his knowledge, I would still be barking as the people's dogs bark! And the servant of God urinated puppies whose shoulders and sides were black and white!

In this treatment, the patient will find bloody urine after receiving the drug, which is a sign of recovery and safety from rabies [23]. However, the quality of this treatment and the drug applied were hidden and kept secret in the *Aswad* family [22], And according to historical reports, it was not taught to others [29].

One of the important points about the application of *Lytta vesicatoria* in prevention of rabies is its side effects which has been noticed by the physicians.

It was generally believed, and the experiences had shown, that the adverse effects of the drug on the urinary bladder and kidneys were significant and that measures should be taken to further reduce its side effects. Therefore, they recommended eating vegetable or animal oils along with the water in which the peeled lentils were cooked [9].

Lytta vesicatoria was known in Greek and Roman medicine and pharmacology, and its healing effects along with dangerous side effects were not hidden from them. However, the use of this drug according to the book of "On Medical Material" (*De materia medica*) and Galen's books and Pliny's Natural History shows that it has not been used in Greece and Rome in the prevention or treatment of rabies [30]. The Greeks and Romans also detoxified the insect's venom by boiling it with boiling vinegar. In the period of Islamic civilization, the use of this insect in the prevention of rabies is evident. The method of mitigating the venom of this insect in Arab and Islamic lands has been different from the Roman method.

In the pre-Islamic period in the Arabian Peninsula, according to the remaining poems, we can believe in the existence of a drug in the prevention of rabies; but it is not clear what the drug was. However, there is a similarity between the symptoms a patient cured by Lytta vesicatoria in its final stage of treatment and the patient's condition mentioned by the pre-Islamic poems (having bloody urine), but one cannot be sure that the medicine used was inevitably the Lytta vesicatoria. If the treatment mentioned in the case of Ibn al-Muhill was by Lytta vesicatoria, it can be said that the origin of this medicine was outside the Arabian Peninsula and probably in Africa. Because the name of the drug and the method used in the treatment are not known, it cannot be judged. The writings of Farāhīdī, 'Īsa ibn Hakam of Damascus, and 'Alī ibn Raban al-Tabarī about the application of Lytta vesicatoria show that none of these writers were the original source. Farāhīdī, who has previously written about Lytta vesicatoria and its benefit in preventing rabies, has relied on previous (possibly oral) sources because he has used the term "it is said (*یقےا*/)".

ⁱIsa ibn al-Hakam also gave meticulous details on how to use *Lytta vesicatoria*, but did not

specify his source for this method of prevention. *Alī ibn Raban Ṭabarī* narrated the medicine extracted from *Lytta vesicatoria* from his father, and if we trust this statement, we must accept that this method of treatment was widespread and that *Tsa ibn al-Ḥakam* was not the only one to know this point.

Well-known and skilled physicians of the Islamic period have generally mentioned *Lytta vesicatoria* as a beneficial, amazing and irreplaceable medicine in the prevention of rabies and hydrophobia. The importance of this medication was so high that a physician of the Islamic period has written about the usefulness of this drug in preventing rabies: "it has a wonderful, clear, and unbelievable benefit which could not be compared with anything else".

Some consider Sayyid 'Ismā'īl Ğurğānī to be the first physician to identify Lytta vesicatoria as an insect with medicinal properties [29]. Although he referred to Lytta vesicatoria as a superb potion [24,31], but it should be noted that centuries before him, this insect and its medicinal properties were known. A contemporary writer in the West has criticized Ibn Sīnā for proposing the use of Lytta vesicatoria to prevent hydrophobia, while this poison is very dangerous and its side effects are similar to those of rabies itself [32]. This criticism does not seem to be acceptable, as the risk of death from being bitten by a rabid animal justifies the use of this drug. In addition, the venom of this insect was mitigated by mixing it with other substances, and the method of its use was such that it showed that the doctor was fully aware of the danger of the drug; but he had to prescribe such a poison to save the patient's life. However, because the toxin of Lytta vesicatoria is dangerous to the bladder, so measures have been taken to protect the bladder. A qualified physician in the Islamic era usually noticed this crucial matter. Another contemporary writer wrote about the knowledge of the Islamic period: "Most of the statements of the physicians of the Islamic period in this regard are a repetition of the Greek material to which little information has been added"[33]. Although the author mentions a few of them; But she was unaware that, firstly, science is gradually evolving and accumulating, and secondly, the repetition and retelling of previous materials in the Islamic period led to the preservation of knowledge and its continuity. Thirdly, what could be more important than the prevention of rabies, which the Greeks and Romans did not mention! Therefore, reducing the scientific efforts of physicians of the Islamic period with such expressions will not be a scientific statement.

Discussion

The use of *Lytta vesicatoria* in the prevention of rabies and the method of mitigating the venom of this insect in this treatment, shows the forward movement in the Islamic period. Before the Islamic period, medicine has no mention of this method of treatment in preventing rabies and hydrophobia. Therefore, it should be considered that in the period of Islamic civilization, along with preserving and continuing the medical tradition of the ancients, new methods were used to control this very lethal disease. Physicians have not limited themselves to preserving

past methods, but have entered new fields of medicine and pharmacology to find better ways to prevent rabies or other diseases.

Since rabies kills sixty thousand people a year, and one of the reasons for the disease is the lack of access to prevention and its high cost to poor countries, it is recommended due to the abundance of this insect in different areas of the world, a clinical trial on a laboratory scale should be conducted about the effectiveness of *Lytta vesicatoria* in preventing rabies. If this test is effective, a cheaper and easier way to prevent rabies can be found.

Conflict of interest

The authors declare that they are no conflicts of interest.

Compliance with Ethical Standards

This article does not contain any studies with human participants performed by any of the authors.

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