



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Use of Saffron Against Dementia and Memory Impairment in Traditional Persian Medicine: A Historical Perspective

Leila Rasi Marzabadi^{1,2} , Reza Mohammadinasab³ , Javad Ghazi Sha'rbaf⁴ , Mostafa Araj-Khodaei^{1,5} , Seyyed Mohammad Bagher Fazljou¹ , Mahnaz Talebi⁶ , Saeed Sadigh Eteghad⁶ 

ABSTRACT

Cite this article as:
Marzabadi LR, Mohammadinasab R, Sharbaf JG, Araj-Khodaei M, Fazljou SMB, Talebi M, Sadigh Eteghad S. Use of Saffron Against Dementia and Memory Impairment in Traditional Persian Medicine: A Historical Perspective. Erciyes Med J 2021; 43(4): 412-6.

In the last century, dementia became one of the most widespread diseases due to the aging world population. Alzheimer's disease is the most common type of dementia. Persian medical literatures have discussed disorders such as forgetfulness and their treatment under the topic "Nesian." Causes of these medical conditions have been also categorized. Poor memory and improving its treatment methods have long been important in traditional medical teaching. For example, saffron is one of the herbs used as a memory enhancer, and it has been cited many times in the related literature. This study sought to consider the history of saffron in the treatment of dementia by examining authentic books of traditional Persian medicine and by describing examples of medicinal compounds affecting saffron-based medications. In reviewing these books, in the eighth century CE, three centuries before Avicenna, Ibn Hakam from Damascus was the first physician who deliberated the role of saffron in the treatment of dementia in his book *Haroniye* (Aaron's book). After him, other great scholars including IbnSina, Ibn Elias Shirazi, and Dawood ibn Omar Antaki developed saffron-based formulas to improve the memory status of patients with forgetfulness.

Keywords: Adult, brain, dementia, historical review, memory booster, memory enhancement, saffron

INTRODUCTION

By definition, dementia is the progressive destruction of cognitive functions in the context of consciousness (1, 2). This disease could be manifested as a set of dysfunctions, including memory impairments, language disorders, psychological and psychiatric changes, and disability in daily activities (3). The World Health Organization estimate that approximately 47 million people worldwide were living with dementia in 2015, which is expected to reach 75 million by 2030 and 135 million by 2050 (4, 5). Dementia has different types. The most common type is Alzheimer's disease, which has affected 10% of people aged >70 years. Alzheimer's disease is a progressive neurodegenerative condition that begins with short-term memory impairment in early stages, followed by cognitive, linguistic, behavioral problems, motor problems, and long-term memory disorders (6–8).

Crocus sativus L., known as saffron, is a plant from the Iridaceae family. This plant is one of the oldest useful spices in the world because of its color, taste, and extensive healing properties. Saffron is known as "red gold" worldwide (9–12). Iran has the largest ecosystem of this plant. Indeed, more than 90% of the world's supply of saffron is planted in Iran (13–16).

To our knowledge, the historical course of the effect of saffron on the treatment of dementia presented in Iranian medical literature has not been explored. Some articles may have discussed the role of saffron in history, but none of them has examined the context of the changes in the use of saffron in dementia in a historical context, especially with reference to Iranian medical books. Therefore, this study aimed to explore the historical importance of saffron in the treatment of dementia by considering ancient Iranian medical literature.

Saffron in Ancient Medicine

Saffron has been the focus of scientists since ancient times (17, 18) Aristotle (384–322 BCE), for instance, mentioned saffron as a fragrant plant (19). In the first century, Galen (129–c.200 CE) defined the properties of saffron in improving gastric diseases (20–22). In Galen's book translated from Syriac and most likely directly translated from Greek into Arabic by Hunayn ibn Ishaq (809–c.873 CE), saffron has been mentioned as a seminal stimulus (22, 23).

In the eighth century, *Haroon's Treatise on Medicine*, or Aaron's book, has mentioned saffron 21 times for treatment of various diseases, including stomachache, as well as for enhancement of liver problems and sexual potency (24–26).

In *Ferdows al-Hikmah fi al-Tib (Paradise of Wisdom)*, the first comprehensive medical book of Islam written in the ninth CE by Ali ibn Sahl Raban al-Tabari (838–c.870 CE), the author of medical resources of three medical

¹Department of Persian Medicine, Faculty of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

²Student Research Committee, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran

³Department of History of Medicine, Faculty of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

⁴Department of Islamic History and Civilization, Faculty of Theology, Azarbaijan Shahid Madani University, Tabriz, Iran

⁵Neurosciences Research Center, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran

⁶Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Submitted
17.11.2020

Accepted
12.01.2021

Available Online
31.03.2021

Correspondence

Mostafa Araj-Khodaei, Faculty of Traditional Medicine, Tabriz University of Medical Sciences, Department of Persian Medicine, Tabriz, Iran
Phone: +989128382094
e-mail: mostafaa33@gmail.com

©Copyright 2021 by Erciyes University Faculty of Medicine - Available online at www.erciyesmedj.com

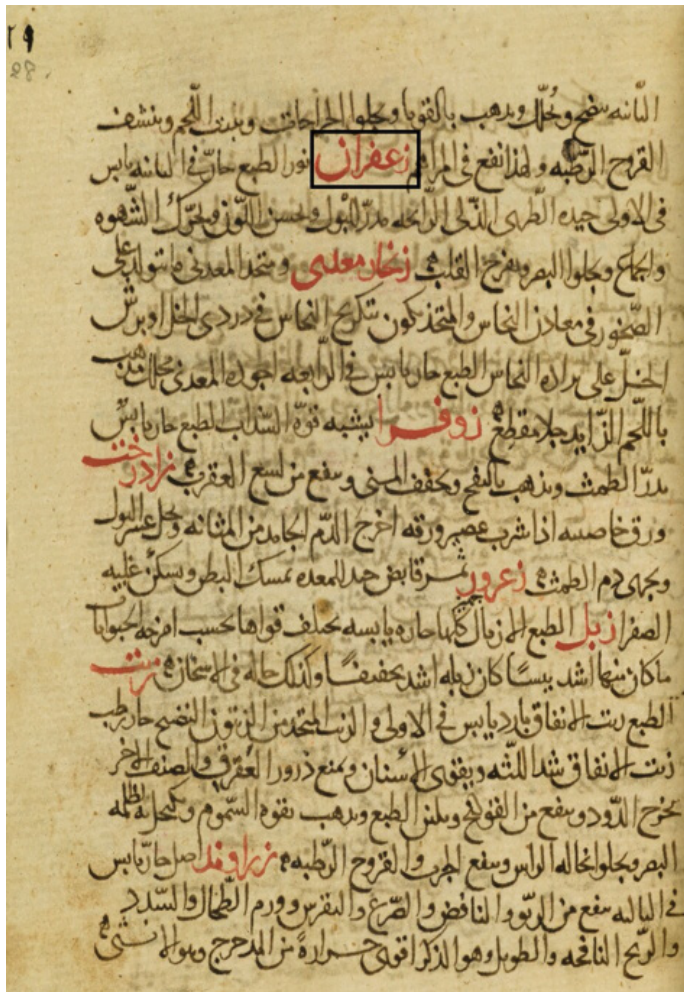


Figure 1. Therapeutic uses of saffron. Source: Taḥṣīl al-ṣiḥḥah bi-al-asbāb al-sittah Tiflīsī, Ḥubaysh ibn Ibrāhīm **British Library: Oriental Manuscripts, Or 8296, in Qatar Digital**

schools of ancient Greece, India, and Iran (27, 28), saffron has been mentioned 109 times, alone or in combination with other herbs, for the treatment of several diseases, including brain diseases (headache and forgetfulness), eye diseases, mouth, teeth, liver, lungs (cough), kidneys, diarrhea, and gout (27, 29, 30).

For many centuries, the efficacy of saffron in skin diseases, eyes problems, headache, melancholia, wound healing, diarrhea, liver and spleen diseases, and depression has been presented in other books about Iranian traditional medicine (19, 31, 32).

Some of the reference books on traditional medicine describing the therapeutic uses of saffron are shown in Figures 1, 2 (33–35). Moreover, recent studies have proved that saffron is clinically useful in improving symptoms of diabetes, Parkinson’s disease, sexual disorders, atherosclerosis, depression, and cancers (36–40).

Early Historical Mention of Saffron to Treat Dementia

In Iranian medical literature, saffron has been repeatedly referred as an important and effective plant in the treatment of dementia. In their books, Iranian physicians (called *tabib* or *hakim*) prescribed different mixtures of saffron to treat dementia. Saffron is one of the



Figure 2. Therapeutic uses of saffron, Canon of Medicin (al-Qānūn fī al-ṭibb). Source: al-Qānūn fī al-ṭibb Avicenna **British Library: Oriental Manuscripts, Or 5033, in Qatar Digital Library**

most common ingredients of most of the prescribed medicines. For example, Masih ibn Hakam from Damascus has mentioned a mixture of different plants including saffron in his book *Haruniye* (41). This appeared to be the first mention of saffron to treat dementia by medieval-century physicians (42–44).

Traditional to Medieval Medicine

In Persian medicine, *nesian* (نسیان) refers to the impairment of memory, thinking, and imagination that is consistent with the modern concept of dementia. This disorder is divided into three categories: deficiency (*noqsan*), absurdity (*botlan*), and disruption

Table 1. Manuscripts citing the use of saffron in boosting memory impairment

Century (CE)	Author	Manuscript	Suggested way of using saffron
8 th	Masih ibn Hakam	<i>Aaron's Treatise</i>	Mixed with cinnamon, halileh, amla, and coconut with honey.
9 th	Ali ibn Sahl Rabban al-Tabari	<i>Ferdows al-Hikmah fi al-Tib</i>	Use alone.
11 th	Avicenna	<i>Canon of Medicine</i>	Mixed with soad kofi, darfelfel, and honey.
14 th	Ibn Elyas Shirazi	<i>Kefaye Mansouri</i>	Mixed with pepper, cinnamon, ginger, oud, senna, coconut, and honey.
16 th	Davood ibn Omar Antaki	<i>Tadhkirat uli al-albab</i>	Mixed with pepper, cinnamon, watermelon, Indian hyacinth, valerian, coconut, incense tree, and honey.
16 th	Mohammad Ibn mohammad abdallah	<i>Tohfe Khani</i>	Mixed with oud, valerian, pepper, cinnamon, etc.
19 th	Mohammad karim ibn Ibrahim Kermani	<i>Daqaiq al-Ilaj fi al-Tibb</i>	Mixed with soad kofi, and extract of fennel.
19 th	Mohammad Sadegh Ali Khan	<i>Makhazen al talim</i>	Smelling saffron.

(*tashvish*) (45, 46). Masih ibn Hakam from Damascus has mentioned a potion to treat dementia in the second volume of his book. In addition to saffron, this potion consisted of cinnamon (*Cinnamomum verum L.*), halileh (*Terminalia chebula L.*), amla (*Phyllanthus emblica L.*), coconut, and honey (47).

Three centuries later, Avicenna (980–c.1037 CE), the greatest physician in the Middle Ages (48–50), has mentioned, in his book *Canon of Medicine*, a mixture of plants, including frankincense, soad kofi (*Cyperus rotundus L.*), darfelfel (*Piper longum L.*), and saffron eventually mixed with honey for the treatment of dementia (19, 51, 52).

In the 14th century, Ibn Elias Shirazi (1320–c.? CE), in his book *Kefaye Mansouri* (Mansouri's Adequacy) referred to a combination of saffron, pepper, cinnamon, ginger, oud, senna, coconut, and honey as an effective drug to mitigate the symptoms of dementia and enhance memory (53). In his book *Khani's Masterpiece* in the 16th century CE, *Tohfe Khani* has also written an article explaining the treatment of dementia. He has also introduced a mixture of saffron, oud, valerian, pepper, cinnamon, etc., to enhance memory (54).

To our knowledge, no medieval physician has mentioned the effects of saffron on the treatment of amnesia, as much as Dawood ibn Omar Antaki (1543–c.1599 CE). In *Tadhkirat uli al-albab*, he has repeatedly emphasized the role of saffron in various compounds for the treatment of amnesia. This physician provided a tested compound consisting of saffron, pepper, cinnamon, watermelon, Indian hyacinth, valerian, coconut, incense tree, and honey for the treatment of amnesia (55).

Three centuries later, Mohammad Karim ibn Ibrahim Kermani (?–1871 CE) also proposed a potion to reduce the symptoms of dementia in his book *Daqaiq al-Ilaj fi al-Tibb (Accuracy of Treatment)*. Furthermore, he introduced herbs such as saffron, soad kofi, and extract of fennel (*Foeniculum vulgare L.*) to strengthen memory and treat dementia (56).

Mohammad Sadegh Ali Khan, the last scholar who lived in India in the 19th century (?–1862), discussed the properties of saffron in the treatment of the dementia. He suggested that even smelling saffron is useful for the prevention and treatment of dementia, similar to aromatherapy (i.e., treatment through smelling

plants) (57). A summary of manuscripts that mentioned the role of saffron in boosting memory is listed in Table 1.

CONCLUSION

Throughout history, saffron has gained a very powerful position in the treatment of dementia. This article also summarized the usage of saffron and its significant effects on dementia with reference to Iranian medical books. According to these books, the use of saffron alone or in combination with other drugs has had a surprising effect on brain function. With the spread of medical science, physicians in different centuries has expanded their knowledge about the beneficial effects of saffron on brain function, especially dementia; as a result, saffron has always been strongly recommended as an effective drug to treat forgetfulness.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – LRM, RM; Design – LRM, RM; Supervision – LRM, RM, JGS; Resource – MAK; Analysis and/or Interpretation – RM, JGS, MF; Literature Search – LRM, SMBF, MT, SSE; Writing – LRM, JGS, MAK; Critical Reviews – SMBF, MT, SSE.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This study is from a Ph.D. thesis and financially supported by a grant from the Neurosciences Research Center, Tabriz University of Medical Sciences (Grant No: 62590).

REFERENCES

- Sattin D, Leonardi M, Picozzi M. The autonomic nervous system and the brainstem: A fundamental role or the background actors for consciousness generation? Hypothesis, evidence, and future directions for rehabilitation and theoretical approaches. *Brain Behav* 2020; 10(1): e01474. [CrossRef]
- Davis DH. Dementia: sociological and philosophical constructions. *Soc Sci Med* 2004; 58(2): 369–78. [CrossRef]
- Neary D, Snowden JS, Northen B, Goulding P. Dementia of frontal lobe type. *J Neurol Neurosurg Psychiatry* 1988; 51(3): 353–61. [CrossRef]
- World Health Organization. Global action plan on the public health response to dementia 2017–2025. Available from: URL: <https://apps.who.int/iris/bitstream/handle/10665/259615/9789241513487-eng.pdf?sequence=1>.

5. World Health Organization. Dementia: a public health priority, 2012. Available from: URL: https://www.who.int/mental_health/publications/dementia_report_2012/en/.
6. Román GC, Royall DR. A diagnostic dilemma: is “Alzheimer’s dementia” Alzheimer’s disease, vascular dementia, or both?. *Lancet Neurol* 2004; 3(3): 141. [CrossRef]
7. Amieva H, Lafont S, Auriacombe S, Rainville C, Orgogozo JM, Dartigues JF, et al. Analysis of error types in the trial making test evidences an inhibitory deficit in dementia of the Alzheimer type. *J Clin Exp Neuropsychol* 1998; 20(2): 280–5. [CrossRef]
8. Román GC. Defining dementia: clinical criteria for the diagnosis of vascular dementia. *Acta Neurol Scand Suppl* 2002; 178: 6–9. [CrossRef]
9. Gismondi A, Fanali F, Labarga JMM, Grilli Caiola M, Canini A. *Crocus sativus* L. genomics and different DNA barcode applications. *Plant Systematics and Evolution* 2013; 299(10): 1859–63. [CrossRef]
10. Ahmadian R, Hosseini F, Salami M. Investigation of Physicochemical Properties and Microbial Contamination of Saffron Style. *J Pharmaceutical and Health Sci* 2016; 4(1): 23–33.
11. Rashed-Mohassel MH. Evolution and botany of saffron (*Crocus sativus* L.) and allied species. *Saffron: Elsevier*; 2020.p.37–57. [CrossRef]
12. Court WE. The formulary of a West Yorkshire pharmacy 1885-1927. *Pharm Hist (Lond)* 1997; 27(1): 2–9.
13. Golmohammadi F. Saffron and its farming, economic importance, export, medicinal characteristics and various uses in South Khorasan Province-East of Iran. *Int J Farm Allied Sci* 2014; 3(5): 566–96.
14. Bazrafshan O, Etedali HR, Moshizi ZGN, MS. Virtual water trade and water footprint accounting of Saffron production in Iran. *Agricultural Water Management* 2019; 213: 368–74. [CrossRef]
15. Alonso G, Zalacain A, Carmona M. Saffron. In: Peter KV, editor. *Handbook of Herbs and Spices*. 1st edition. Woodhead Publishing, Elsevier; 2012.p.469–98. [CrossRef]
16. Shahnoushi N, Abolhassani L, Kavakebi V, Reed M, Saghaian S. Economic analysis of saffron production. *Saffron: Elsevier*; 2020.p.337–56. [CrossRef]
17. Basker D, Negbi M. Uses of saffron. *Economic Botany* 1983; 37: 228–36. [CrossRef]
18. De Mastro G, Ruta C. Relation between corm size and saffron (*Crocus sativus* L.) flowering. *Int Symposium Med Aromatic Plants* 1993; 344: 512–7. [CrossRef]
19. Hosseinzadeh H, Nassiri-Asl M. Avicenna’s (Ibn Sina) the Canon of Medicine and saffron (*Crocus sativus*): a review. *Phytother Res* 2013; 27(4): 475–83. [CrossRef]
20. Francis S, Ramandi MT. Properties of Saffron. In: Francis S. *Crocolgia—A Detailed Study of Saffron, the King of Plants* (Brill’s Studies in Intellectual History / Brill’s Texts and Sources in Intellectual History 22). 1st edition. Brill; 2020.p.65–8. [CrossRef]
21. Ansari AP, Ahmed NZ, Wadud A, Arif M, Khanday S. Ilaj bil Ghi-za (Dietotherapy): A core mode of Unani treatment. *J Advanced Res Pharmaceutical Scie & Pharmacol Interven* 2018; 2(1): 27–35.
22. Sadeghi S, Ghaffari F, Alizadeh M. Al-Masā’il fi al-tibb: Hunain ibn Ishāq’s historic medical text with a distinctive style of Islamic medical education. *J Med Biogr* 2021; 29(1): 29–34. [CrossRef]
23. Ishaq H, Rayyan MAA, Arab MM, Musa YM. Al-masa’il fi l-tibb li-l-muta’allimin. *Dar al-Yami’at al-Misriyya*; 1978.
24. Saad B, Said O. *Greco-Arab and Islamic herbal medicine: traditional system, ethics, safety, efficacy, and regulatory issues*. 1st edition. John Wiley & Sons; 2011. [CrossRef]
25. Nabavi SM, Suntar I, Barreca D, et al. *Phytonutrients in Food*. 1st edition. From Traditional to Rational Usage: Elsevier Science; 2019.
26. Langermann YT. From My Notebooks: Masīh bin Ḥakam, a Jewish-Christian (?) Physician of the Early Ninth Century. *Aleph* 2004; 4: 283–97. [CrossRef]
27. Meyerhof M. Ali at-Tabari’s “Paradise of Wisdom”, one of the oldest Arabic Compendiums of Medicine. *Isis* 1931; 16: 6–54. [CrossRef]
28. Ardalan M, Khodadoust K, Mostafidi E. A Review of Ferdous al-Hekma fil-Tibb by Ali ibn Raban Tabari. *J Med Ethics Hist Med* 2015; 8: 7.
29. Rabban al-Tabari AB. *Firdous al-Hekmah (Paradise of Wisdom)*. Edited by Siddiqi MZ. Berlin: The Gibb Memorial Trust; 1928.p.321–5.
30. Majeed A. How Islam changed medicine. *BMJ* 2005; 331(7531): 1486–7. [CrossRef]
31. Yousefi M, Shafaghi K. Saffron in Persian traditional medicine. *Saffron: Elsevier*, 2020.p.393–404. [CrossRef]
32. Chishti GM, Chishti HG. *The traditional healer’s handbook: a classic guide to the medicine of avicenna*. Inner Traditions/Bear & Co; 1991.
33. al-Qānūn fi al-ṭibb, Avicenna, British Library: Oriental Manuscripts, or 5033, in Qatar Digital Library. Accessed December 13, 2020.
34. al-Mūjiz fi ‘ilm al-ṭibb, Ibn al-Nafis, ‘Alī ibn Abī al-Ḥazm, British Library: Oriental Manuscripts, or 5659, in Qatar Digital Library. Accessed December 13, 2020.
35. Taḥṣīl al-ṣiḥḥah bi-al-asbāb al-sittah, Tiflīsī, Ḥubaysh ibn Ibrāhīm, British Library: Oriental Manuscripts, or 8296, in Qatar Digital Library. Accessed December 13, 2020.
36. Christodoulou E, Kadoglou NP, Kostomitsopoulos N, Valsami G. Saffron: a natural product with potential pharmaceutical applications. *J Pharm Pharmacol* 2015; 67(12): 1634–49. [CrossRef]
37. Razavi BM, Hosseinzadeh H. Saffron: a promising natural medicine in the treatment of metabolic syndrome. *J Sci Food Agric* 2017; 97(6): 1679–85. [CrossRef]
38. Leone S, Recinella L, Chiavaroli A, Orlando G, Ferrante C, Leporini L, et al. Phytotherapeutic use of the *Crocus sativus* L. (Saffron) and its potential applications: A brief overview. *Phytother Res* 2018; 32(12): 2364–75. [CrossRef]
39. Lopresti AL, Drummond PD. Saffron (*Crocus sativus*) for depression: a systematic review of clinical studies and examination of underlying antidepressant mechanisms of action. *Hum Psychopharmacol* 2014; 29(6): 517–27. [CrossRef]
40. Al-Andalusi S. *Science in the medieval World.* Book of the Categories of Nation. University of Texas Press, 1991.
41. Langermann YT. Transcriptions of Arabic treatises into the Hebrew alphabet, an underappreciated mode of transmission. In: Jamil Ragep F, Ragep SP, editors. *Tradition, Transmission, Transformation*. Brill; 1996.p.247–60.
42. Klein-Franke F. Al-Kindi. *History of Islamic Philosophy, Part I* 1996.p.165–77. [CrossRef]
43. Klein-Franke F. Al-Kindi. *History of Islamic Philosophy* 2013; 1: 165.
44. Shirbeigi L, Dalfardi B, Abolhassanzadeh Z, Nejatbakhsh F. Dementia Etiologies and Remedies in Traditional Persian Medicine; A Review of Medicinal Plants and Phytochemistry. *Curr Drug Metab* 2018; 19(5): 414–23. [CrossRef]
45. Ahmadian-Attari MM, Shirzad M. Physiopathology of Dementia in Iranian Traditional Medicine. *J Evid Based Complementary Altern Med* 2016; 21(4): 253–4. [CrossRef]
46. Damascus MIHo. *Aaron’s treatise*. Tehran: Institute of Medical History, Islamic and Complementary Studies, Iran University of Medical Sciences; 2009.
47. Khan A. *Avicenna (Ibn Sina): Muslim physician and philosopher of the eleventh century*. The Rosen Publishing Group, INC; 2006.
48. Jacquart D. Islamic pharmacology in the middle ages: theories and substances. *European Rev* 2008; 16(2): 219–27. [CrossRef]
49. Afshar A, Steensma DP, Kyle RA. Ibn Sina (Avicenna): The “Prince of Physicians”. *Mayo Clinic Proceedings: Elsevier* 2020; 95(3): E31–2.
50. Bakhtiar L, Gruner OC, Shah MH. *The Canon of Medicine (al-Qānūn*

- Fr'l-tıbb): Abjad Book Designers & Builders, 1999.
51. Smith RD. Avicenna and the Canon of Medicine: a millennial tribute. *West J Med* 1980; 133(4): 367–70.
 52. Shirazi EE. *Kefaye Mansoori*. 1st ed. Iran University of medical sciences. Tehran 2003.p.280.
 53. Ubaidullah bin Mahmud U: tohfe Khani, correction: mirtoteil A. Institute of Historical Studies, Islamic and Complementary Medicine. 1357.p.115–3.
 54. Bray J. Dawud ibn 'Umar al-Antaki. In: Lowry JE, Stewart DJ, editors. *Essays in Arabic Literary Biography II:1350-1850*. Harrassowitz Verlag. Wiesbaden; 2009.p.48.
 55. ibn 'Umar Al-Anṭākī D. *Tadhkirat ulī al-albāb wa-al-jāmi' lil-'ajab al-'ujāb; al-Nuzhah al-mubhijah fī tashhīdh al-adhhān wa-ta'dīl al-amzījāh*. Institute for the History of Arabic-Islamic Science at the Johann Wolfgang Goethe University, 1997.
 56. Kermani MK. *Daqaiq al-Ilaj fi al-Tibb*. Saadat. Kerman; 1983.
 57. Khan MSA. *Makhazen al Taalim*. (Treasures of education). India-Delhi: Press Farooqi; 1905.