

### URINARY CALCULUS FORMATION THEORY and TREATMENTS

### DESCRIBED BY AHMED ÇELEBI IN 15th CENTURY TURKEY

### Prof. Dr.Nil Sari,

Biruni University, Head of Medical History and Ethics Department, İstanbul, Turkey, Biruni Faculty of Medicine board member. President of the Health History Museology Association. Founder of the Cerrahpasha Medical School Medical History Museum.

DOİ: 0000-0002-4935-8658

Correspondence: <u>hsari@biruni.edu.tr</u>

Keywords: urinary calculus, Turkish medicine,  $\overline{Ahi}$  Çelebi,  $15^{th}$  century, urolithiasis, renal stones, history of medicine

#### Summary

 $\overline{Ahi}$  Ahmed Çelebi, chief physician to three Ottoman sultans, provides detailed information about the formation and treatment of kidney and bladder stones in his work titled "Treatise On the Urinary Calculus in the Kidneys and the Bladder", which he wrote in Turkish in 1487. The author's statements and his way of handling issues indicate that he is an experienced and attentive physician. It is remarkable that some information given in this book is similar to today's.

After thoroughly describing the aetiology of stone formation in the urinary tract,  $\overline{Ahi}$  *Çelebi* discusses the incidence of urinary calculi according to age and gender. As per principles of Islamic medicine, emphasis is placed on preventative measures. Hence, prophylaxis against urinary calculus formation, i.e. avoiding food considered to be the cause of calculus formation and intake of prophylactic nutrients, is discussed in detail.

Signs and symptoms of kidney and urinary bladder calculi, as well as differential diagnosis are discussed. Medical therapy is discussed and recommended. A description of multi-action medications for relief of specific symptoms such as pain, fever and hematuria is provided. Instruments used in the treatment of a vesical calculus such as syringes, catheters, lithotrites are described, as well as instructions in their use. *Çelebi* also mentions the case of a patient who devised a tool to relieve his own vesical calculus.

#### Introduction

*Āhī Çelebi Aḥmed b. Kemāled din Sirvānī* (1432-1524) was a Turkish physician of the fifteenth and sixteenth centuries.[1] He was chief physician to three Ottoman sultans - first *BāyezidII*, then*Yavuz Sulṭān Selīm* and finally, *Ķānūnī Sulṭān Süleymān*. His monograph "Treatise on the Urinary Calculus in the Kidneys and the Bladder" (*Risāletü'l kilyeteyn ve'l-mesāne* or *Risāle-i hasātü'lkilyeve'l-mesāne*) is dated 893H/1487-8 CE and is written in the Turkish language in Arabic script. The 180-page (80 folios) work contains ten chapters. To research this article, the copy registered at number 1491 in the *Baġhdādlı Wehbī Efendi* section of the *Süleymāniye Library* was studied. Comparison of this text and other ancient texts on similar subjects is beyond the scope of this article.



Thetreatisecomprises interesting theoretical discussions as well as practical knowledge and recommendations. The scientific method and complex devices for diagnosis and treatment did not exist in  $\bar{A}h\bar{i}$  *Çelebi*'stime. Instead, medical knowledge and practice was based on empiricism, of which the theory of humours was a part. This was understood as a scholarly mechanism of interpreting empirical evidence. As well as referencing the common understanding of humours,  $\bar{A}h\bar{i}$  *Çelebi* occasionally cites his own experiences as evidence in his writing.

This treatise was previously transferred from Arabic letters to Latin letters, however some incorrect readings were made and the text was not analyzed and discussed. [2] In another study on Turkish language, the text was evaluated in terms of language characteristics that is spelling, phonetics and morphology. [3] In this study, theoretical and practical information written in the treatise are compiled under specific subject headings and considered in terms of evolution of medicine. The folios of the manuscript from which the information is transferred are given in round brackets at the end of the relevant section. In order to draw attention to common points with today's medical information, relevant publications to some of the topics are cited as sources and brief commentaries are argued within the framework of today's knowledge. The text can be discussed further in relation with modern medicine.

## AETIOLOGY OF URINARY TRACT CALCULUS FORMATION

 $\overline{Ahi}$  *Çelebi* describes the formation of renal stones with the humoural theory. He states that any humour (blood, phlegm, yellow bile, black bile) that decomposes has a tendency to contribute to calculus formation and that decomposed humours remaining in the kidneys give rise to stasis and humidity occurs, causing calculus formation. (6b) Present-day studies reveal that urinary stasis does promote stone formation and humidity is a risk factor for urolithiasis.[4,5]

It is claimed in the treatise that calculus formation is a constitutional disturbance and occurs mostly in obese individuals who eat to excess, having fat and humid bodies. (7a) [6]  $\overline{Ahi}$  *Çelebi* writes that calculi appear mostly in the kidneys of the obese (pyknic body type), as obesity can cause the urinary tract and orifices to narrow. Calculus formation in the kidneys is rarely observed in individuals who have asthenic body types. In the

Vol 7 - No. 3 | April 2021 | www.jbima.com

asthenic, calculi appear in the bladder. As the lumen of their tract is larger, the humour that causes calculi collects in the urinary bladder, as it does not remain within the lumen of the ureter. (6ab) Although modern medicine does not ascribe completely to this understanding, studies do report causal relationships between kidney stone formation and metabolic syndrome and/or central obesity, with a greater risk of uric acid stones in those with abdominal obesity[7].

The role of gender and age in stone formation is also discussed in the treatise. It is asserted that the incidence of calculus formation is higher in boys malnourished until adolescence. A recent study puts forth that "vesical calculi are commonly seen in developing countries in pediatric age group patients belonging to poor economic status." [8] As to Ahi Çelebi, he says that if a boy is given animal or breast milk of the bilious humor, it will cause the internal organs of the boy to become "dry" and dense which causes calculus formation. If the "nature of the milk" is of the phlegm humour, the boy's urine will be denser. The accumulation of dense humor leads to heat in the urinary bladder inducing calculus formation. (6b) Does calcium intake by drinking milk increase formation of calcium stones children? Recent studies discuss the effects of different types of milk and the volume of milk intake on formation of stones. [9]

Were calculi particularly common in the urinary bladder of boys during the Ottoman period? Certificates of consent for vesical calculus surgery are encountered frequently in court registers as the most frequent surgical procedure, and the contracts of consent concerning urinary calculus surgery are most frequently related to boys. There is a case described of a father who signed the contract of consent for his son's operation to reduce or extract a stone. He is described as a boy or a small boy with a stone in his groin/urethra/urinary bladder.[10] Perhaps the incidence of calculi was so high as a result of surgical infection because of circumcision in some cases. Modern studies have shown that urinary tract infection can promote urinary stasis and increase the risk of stone formation.[11, 12]

 $\overline{Ahi}$  *Çelebi* notes that vesical calculi do appear in girls, although calculi are rarely formed in the urinary bladder of women because of the anatomy of the female urinary tract. The vesical neck in women is free, the urethra is very short and the orifice open and near to the exterior. If a humor flows into the bladder, it is expelled quickly. Women may be able to feel the calculus with a finger.



Vol 7 - No. 3 | April 2021 | www.jbima.com

(6b) Modern data shows that the incidence of kidney stones in women is about half that of men.[12, 4]

 $\overline{Ahi}$  *Çelebi* notes a relationship between lack of sexual intercourse or non-ejaculation and calculus formation. He states that "having desire and libido for sexual intercourse but lack of sexual intercourse, talking on erotic subjects or love making but lack of ejaculation." can contribute to calculus formation. (7b) It is difficult to

explain this view of  $\overline{Ahi}$  *Çelebi* in light of ourcurrentunderstanding on this, but a neurological defect that disrupts erection or ejaculation may also affect urine excretion as an autonomic function and left over urine in the bladder may cause stone formation. There are studies on the influence of sex hormones and calculus formation secondary to genital infection which may also cause ejaculatory duct obstruction. [13]

Folios 33b and 34a, the beginning of thr section on the treatment of urinary stone cold in nature, from the "Treatise on the Urinary Calculus in the Kidneys and the Bladder" of Ahi Ahmed Çelebi

## PROPHYLAXIS AGAINST URINARY CALCULUS FORMATION

 $\bar{A}h\bar{i}$  *Çelebi* discusses prophylaxis of urinary stones at length. He recommends three action to take for prevention of calculi.

I. Avoid food and drinks causing urinary calculus formation

II. Change attitude and behavior

III. Evacuate substances that cause formation of calculus. Today's guidelines often provide similar recommendations. [14]

#### **Nutrients That Cause Calculus Formation**

 $\bar{A}h\bar{i}$  Çelebi discusses the types of urinary stones with reference to the theory of elements. He suggests that

kidney stone prophylaxis should differ depending on the specific type of element causing the stoneand its characteristics. The relationship between nutrition and stone formation is explained at length. Malnutrition with food which prevents removal of intestinal gas, consecutive meals, stomach indigestion (gastritis), liver failure, kidneys 'hot' in nature and spoiled unripe humors are cited as causes of urolithiasis. (17a-27b, 29b-33b)

Food and drink that may lead to calculus formation is listed including red meat (beef meat and fat, lamb, lamb head, camel meat, trotter, roasts, kabobs), animal products (spoiled cow milk, rice with milk), raw fruit (bitter orange, citrus, pear, apple) garlic, onion, spinach, vermicelli, shredded wheat, starch pudding, turbid water and old, intense wine. When turbid water or dense winesyrup mix with other food in the stomach, a sediment is



formed which contributes to calculus formation. Contemporary studies show that dietary factors such as animal protein and some fruits and vegetables influence the pH of urine, causing further crystallization and increasing the risk of urinary stone formation.(7a-8a, 13a) [12, 5]

#### **Measures To Prevent Kidney Stones**

Dietary measures are mentioned as prophylaxis against calculus formation.  $\overline{Ahi}$  *Çelebi* recommends certain foods and avoiding heat. Exercise (such as running) and taking a warm bath or engaging in sexual intercourse after a meal and lying on a warm mattress should be avoided. This is to prevent excessive sweating and heat in kidneys, according to the humoural theory (13b, 14a, 16b, 17a) Today, heat-induced sweating is discussed as a cause of stone formation.[15, 16]

If water is drunk in the middle of the meal from time to time, or drunk on an empty stomach, stones will not occur in the kidney, but it is wrong to drink water all the time just because it's a good measure, for various harms arise from the excess of good precaution. (16b) Today, it is suggested that, "uncomplicated stones can be managed conservatively with adequate fluid intake."[12, 14]

 $\overline{Ahi}$  *Çelebi* suggests that a diet of "easily digestible food" can prevent stone formation. The intake of animal protein promotes calculus formation, but some sources are lower in fat and are less calorie-dense. Thus, intake of certain sources of protein is recommended including white meat like young chicken, house sparrow, pigeon, partridge, swallow and francolin/grouse and red meat like sheep, goat and rabbit. (14a)

A diet of fruit and vegetables, for example, fig, red grape, celery, carrots, Swiss chard, mallow, peppermint, common fennel is recommended.  $\overline{Ahi}$  *Çelebi* provides recipes that will prevent stone formation. (14b-15a) Today we know that the acidity or alkalinity of fruits and vegetables (their varieties, method of cooking and processing) have an effect on stone build-up. [17]

 $\overline{Ahi}$  *Çelebi* advises that patients should take food and drugs that promote diuresis as a strong stream of urine may allow the calculus to pass. Examples of recommended diuretics are Capparis, chickpea, sheep sorrelroot, asparagus seedand root, and cyperus longus. (55b)[18]

 $\overline{Ahi}$  *Çelebi* also recommends vegetable, fruit and seed oils (walnut oil, almond oil and peanut oil), seeds (caltrops

and fenugreek), and plants (spurge /euphorbia and Chinese rhubarb root) as laxatives and to promote renal health. (67a)

Vol 7 - No. 3 | April 2021 | www.jbima.com

#### SIGNS AND SYMPTOMS OF KIDNEY CALCULI

Signs and symptoms of kidney stones are described in detail in the treatise, such as a continuous feeling of heaviness felt around the kidney and a pain that is exacerbated by eating to excess. The pain increases when faecal matter collects in the intestines and is relieved by defecation. Sometimes, testicular pain or thigh paresthesia are signs of a calculus in the ipsilateral kidney. Patients can also report abdominal colic. In "overheated kidney disorder" patients experience fever and rigors. (10a-10b, 11a, 21a)

 $\overline{Ahi}$  Çelebi notes the differential diagnosis between renal colic and abdominal pain. Abdominal pain is felt around the peri-umbilical region but renal pain tends to be felt in the back, radiating to the side and is local. Sometimes it can be associated with thigh numbness, which is not observed in gripe. (9b, 10b-11a)

There is frequent mention of urine inspection in a flask and  $\overline{Ahi}$  *Çelebi* describes the approach to uroscopy and its diagnostic relevance. He states that in the presence of calculi, the normal strength of the urinary stream falters as the dense substances in the urine are left back in the kidneys. Dark urine without pain is evidence of recent calculus formation. This is especially true if the sign appears in old age. Yellowish and reddish sand in urine is a sign of kidney calculus. (9a-9b, 10a-10b)

# SIGNS AND SYMPTOMS OF URINARY BLADDER CALCULI

 $\overline{Ahi}$  *Çelebi* then describes the presentation of urinary bladder calculi. He states that if there is pain and heaviness in the loins radiating inferiorly towards the thighs, it is evidence that the calculus has descended from the kidneys into the urinary tract. Later, if the pain is alleviated, the stone has descended into the urinary bladder. When the stone is in the bladder, pain, heaviness and itching appear at the base of the penis. Sometimes pain is felt in the groin. The patient frequently handles his groin involuntarily. White or grey urinary sediment is a sign of urinary bladder calculus. (9b, 10a, 11a-11b).

Most patients with a bladder calculus have difficulty in urination and feel post-urination urgency. Sometimes the patient urinates abruptly, and this happens often after



urination. In these patients the urinary bladder calculus is large and tortuous. A man with a bladder calculus will feel numbness in his penis while walking, with pain at the base of the penis while running. While walking fast or jumping causes pain, lying in the foetal position relieves the pain at the base of the penis. When the stone reaches the bladder neck, it becomes painful and prevents urination. A large, heavy stone can make defecation difficult and can sometimes cause rectal prolapse. (11b, 12a-12b, 13a)

There can sometimes be two or more calculi in the urinary bladder. During exercise there is traction between the stones and as a result the urine can contain a white sandy sediment which settles at the bottom of the flask. If there is much sand, this indicates that the calculus is soft and disintegrable. If there is very little or no deposit, it indicates that the calculus is hard. (12b-13a)

#### MEDICAL TREATMENT OF KIDNEY AND BLADDER CALCULI

Medication is indicated depending on the type of kidney stone and the characteristics of the patient's urine. Several formulas are prescribed for the treatment of pain, inflammation, bleeding, fever, obstruction and urinary tract infections . (44a-44b, 46b-47a, 54a)

If the pain cannot be relieved while the calculus is stuck in the urinary tract, analgesics, sedatives, tranquilizers and soporifics are indicated.  $\overline{Ahi}$  *Çelebi* advises the use of Indian hemp, opium, olibanum, radish pyrethri romani, henbane, mandrake and lettuce seeds. (74b-75a)

Prescriptions given in the text comprise drugs with multiple medicinal effects. For example, one formulation is composed of terra Armenica, olibanum, dragon gum, limestone, melon seed and Plantago lanceolate. Each of the drugs in this tablet treat specific symptoms caused by the stone, with diuretic, analgesic, sedative, antiseptic, styptic, antipyretic and anti-inflammatory effects.(45a-45b) Similarly, a resin–balsam formulation consists of pine, spruce, balsam tree, dragon gum, gommaTurca and sandalwood, altogether having antiseptic, analgesic, styptic, anti-inflammatory and analgesic effects.

*Āhī Çelebi* recommends inorganic nutrients (both metallic and non-metallic minerals (fossilized organic substances) having active ingredients that prevent certain kidney stones, such as lapis Judaicus[19], pumice, oilstone, whetstone, khwarezm bead and spumas salis(63b,73b).Today we know that these minerals are sources of elements such as magnesium and calcium

which are recommended as nutritional supplements for prevention of different types of kidney stones, having an antilithiatic effect.[6]

### Administration of Pharmaceutical Preparations to Fragment and Disintegrate Stones of the Urinary Tract (Lithotripsy)

When a kidney stone does not pass on its own due to its size or position,  $\bar{A}h\bar{i}$  *Çelebi* would administer drugs that might create stone fragments "small enough to be expelled in the urine" both orally andby irrigation of the bladder. Ingredients of a recipe for this purpose are unshelled cucumber seed, unshelled melon seed, unshelled pumpkin seed, celery seed, fennel seed, pumice stone or burned glass. These would be pounded in a mortar and mixed with vinegar and honey. This was to be drunk on an empty stomach. (28a-28b). There are other recipes included that reduce the kidney stone and promote its descension to the bladder in the form of slime.(34b)

Some interesting calculus reducing prescriptions are given under separate headings. Below, I give examples of these calculus reducers.

Scorpion oil: rhubarb, gentian, willow, capparis/caper root bark, 10 dirham each are pounded together.130 dirham almond oil is added and all are stirred. The mixture is put in a bottle and left in the sun for a week. Then the herbs are filtered. Ten live scorpions are added to this oil. The bottle is closed and hanged against the sun for two weeks. This is drained, the scorpion are thrown the oil is administered. (41b-42a). away and Dried he-goat /buck blood: A four year old buck is slaughtered. After the animal bleeds for a little time, blood is taken and put in a clay pot. After coagulation, pieces of blood are put on a sieve, covered with a cloth and left in the sun. It must be dried completely, without humidity or dust. At one intake three dirhams can be given. (42a-b) Burned glass: White Damascus silica frit, yet not wet, is put in an iron scoop and held on a fire. When it gets red hot, it's left in cold water. Then again it's held on a fire, when it gets red hot, it's again left in cold water. Melted frit is collected. This process is repeated until the product is in such a state that it could be pounded into powder in a mortar. (43b-44a)

#### Syringe for Vesical Irrigation

 $\bar{A}h\bar{i}$  Çelebi describes a syringe for bladder irrigation, which he named as "suatacak" in Turkish. Aprobeis



Vol 7 - No. 3 | April 2021 | www.jbima.com

inserted into a tube fit to the urethra. A piece of cloth is wrapped on the forepart of the probe inserted into the tube. A thinner tube is fitted on the tip of the original tube. Then the thinner tube is dipped into the fluid needed and the probe is pulled back. Hence fluid is drawn into the original tube. Then the thin tube is inserted into the external urethral orifice. Water is carried gradually into the urinary bladder. (45b- 46b)

Various bladder irrigants are outlined. A decoction prescribed for irrigating the bladder with a syringe is described. It consists of violet, lettuce, cucumber, sesame and gomma Turca (cherry tree mucilage) with resulting antifungal, sedative, analgesic, anti-inflammatory, diuretic and lubricating effects.(45b)[18]

 $\overline{Ahi}$  *Çelebi* states that the treatment for suppuration as a result of calculi obstructing the urinary tract is irrigation by means of a clyster. A prescription for the treatment of urinary tract infections is composed of white lead, terra sigillata (sealed clay tablets), dragon's blood resin, opium and cannabis sativa. This is mixed and pounded, then dissolved in Plantago major juice and rose water. These ingredients have several therapeutic effects including diuretic, anti-inflammatory, antipyretic, analgesic and antispasmodic actions.(45a)

#### A Case of Urine Retention

*Āhī Çelebi* writes about two devices developed by a patient known as AmirAli Keyvan Bey suffering from bladder stones. A renal calculus descendedand became stuck in his bladder. He could only pass two or three drops of urine with difficulty. In terms of treatment, some doctors recommended a massage on the penis. Others said the meatus of the penis must be widened by an incision to give way for the calculus. Others again recommended dressing. Diuretics were of no use. Tired of the futile interventions of useless physicians, Amir Keyvāntook it upon himself to devise a solution, inventing an instrument touse on himself. He first designed a catheter. He made a slender tube/cannula of silver. One end of the tube was sound, the other end was narrower with holes like a flute. When he felt the urge to urinate, he would insert the tube from its thinner end through the urethra and push the calculus back. Thus he was able to urinate through the holes before withdrawing the tube.(48b, 50a-50b)

But  $\overline{AmirKeyvan}$  wanted to be completely free from this trouble. He made a second instrument which was a lithotrite. He constructed a clamp – a pair of steel pincers, with their ends like short shafts. The rivet of the

pincers was at the base of the shafts. Whenever the clamp was opened, its tip widened. One day he inserted the pincers through the urethra into his bladder. When it met the calculus, he opened the clamp - the tip opened, but the ends were designed to only widen slightly as to cause minimal discomfort. He held the stone firm with the short tip, and the stone crushed into pieces there and then he was able to pass urine. (51a-51b)

# Surgical Procedure for The Removal Of Bladder Stones (Lithotomy)

*Āhī Çelebi* advises on important considerations before practicing lithotomy and warns the practitioner. He says that if the stone is of considerable size and does not flow out of the bladder with the drugs and medical preparations mentioned, there is no other measure that will help but lithotomy. However, it is likely to cause harm. It's rarely safe and there is a high chance that the patient will not survive. Some ancient physicians said that they even excised the kidney stone from the back, but he notes "There is no one who did this in the present time. It's too dangerous." However, he states that incision of the bladder is easier and safer and that whoever wants to do this operation should consider three issues thoroughly. Firstly, it is necessary to pay attention to the age of the patient. Very young or very old patients cannot survive surgery. Secondly, one should be careful about the stone size. If the stone is small, it escapes from the finger and is difficult to find and remove, causing great trouble for the patient. If the stone is too large, the surgical wound will be great in size. If the stone is long, the incision should be made superior to the stone to minimise the size of the surgical wound. Finally, one should evaluate the patient's pain intensity. If the patient suffers too much and is tired of his troubles, he will be willing to endure the inconvenience of surgery to be rid of it. If the patient's pain is mild, they will not want to undergo surgery.

 $\overline{Aht}$  Çelebi says, "The situations we have mentioned in this chapter are the necessary skills for the physician. Surgical incision is an order of surgery and it requires observation.Since it is difficult to address it in a book, it is not mentioned in this short treatise.(52a-55b)

#### Conclusion

The evidence and commentary that  $\overline{Ahi}$  *Çelebi* presented more than 500 years ago in a period before modern medical technology suggest that he was a wise and experienced physician. His discussion on the aetiology, prophylaxis, presentation, prognosis and treatment



methods of urinary tract stones indicate that he made practical and effective use of the scholarly methods of his time - observation, visual inspection, physical examination, analogy, classification, discussion - most skillfully. This work should invite further detailed study so that its place in medical history can be fully acknowledged.

#### References

1. Kalem T. Ahi Çelebi'ninhayatıveeserleri. MScthesis, UşakUniversityInstitute of SocialSciences, Uşak 2017.

2. ErkunS., Ahi Ahmed b. Kemaleddin el-mütetabbib, risaletü'l-kilyeve 'l-mesane, İstanbul 1948.

3. Yurdakul Y. Risale-ihaşatü'l-külyeve'lmeşanegiriş-inceleme-metin-sözlük-tıpkıbasım. <u>MScthesis</u>,SüleymanDemirel University Institute of Social Sciences, Isparta, 2001.

4. Morton AR, Iliescu EA, WilsonJWL. Nephrology: 1. Investigation and treatment of recurrent kidney stones. CMAJ. 2002 Jan 22; 166(2): 213–218. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PM C99277/.

5. Pletrow PK, KarellasME. Medical management of common urinary calculi. SA FamPract 2007; 49/3: 44-48.

6. FrassettoL,Kohlstadt I. Treatment and prevention of kidney stones: an update. Am Fam Physician. 2011 Dec 1;84(11):1234-1242.

7. Hess B. Metabolic syndrome, obesity and kidney stones. Arab J. Urol., 2012 Sept;10(3):258-264.

8. Acharya H, Dhende NP, Mane SB, Obaidah A. Posterior urethral valves with vesical calculus: A rare association.J Indian AssocPediatr Surg. 2009 Jul-Sep; 14(3): 115–116. Available from: www.ncbi.nlm.nih.gov > pmc.

9. Hossain, RZ, Ogawa Y, Morozumi M, Hokama S, Sugaya K. Milk and calcium prevent gastrointestinal absorption and urinary excretion of oxalate in rats. Front. Biosci, 2003 May 1; 8: 117-125.Available from: https://www.researchgate.net/publication/10800742

10. Sarı N. Medical ethics regarding pediatric surgery during the ottoman period. 36th International Congress

Vol 7 - No. 3 | April 2021 | www.jbima.com

on the History of Medicine Proceedings. Tunis-Carthage, September 6th-11th 1998, 133-138.

11.Miano R, Germani S, Vespasiani G. Stones and urinary tract infections.Urol Int. 2007; 79 Suppl1:32-6.

12. Parmar MS. Kidney stones, BMJ. 2004 Jun 12; 328(7453): 1420–1424.

13. Yagisawa T, Ito F, Osaka Y, Amano H, Kobayashi C, Toma H. The influence of sex hormones on renal osteopontin expression and urinary constituents in experimental urolithiasis.J Urol. 2001 Sep;166(3):1078-82. Available from: https://pubmed.ncbi.nlm.nih.gov/11490302/

https://publicd.neoi.min.nm.gov/11490502/

14.Fontenelle LF, Sartı TD. Kidney Stones: Treatment and Prevention, Am Fam Physician. 2019 Apr 15;99(8):490-496.

15.Gul Z, MongaM.Medical and dietary therapy for kidney stone prevention. Korean J Urol. 2014 Dec; 55(12): 775–779.

16. Fakheri R. J,Goldfarb DS. Ambient temperature as a contributor to kidney stone formation: implications of global warming. Kidney Int., 2011 June; 79(11): 1178-1185. Available from:

https://doi.org/10.1038/ki.2011.76.

**17**.Han H, Segal AM, Seifter JL, Dwyer JT. Nutritional management of kidney stones (nephrolithiasis).ClinNutr Res. 2015 Jul; 4(3): 137–152. Published online 2015 Jul 31. doi: 10.7762/cnr.2015.4.3.137

18.BaytopT.Türkiye 'de bitkilerle tedavi geçmişte ve bugün. Nobel Kitabevleri 1999, İstanbul.

19.Mustehasan, Azhar M.Hajarul yahood (Jew'stone) anti-urolithiatic Unani mineral drug – review.World J. Pharm. Res., 2020;9(6): 1127-1133