

Ibn-Sina's Life and Contributions to Medicinal Therapies of Kidney Calculi

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Ibn-Sina (commonly known as Avicenna) is one of the most famous and influential scientists in the history of medicine. The *Canon of Medicine*, which is his most celebrated book in medicine, presents a summary of all the medical knowledge of his time. Ibn-Sina wrote a complete section about kidney calculi in his book. Totally, 65 herbal, 8 animal, and 4 mineral medicines are mentioned in the *Canon of Medicine* as beneficial drugs for destructing, expelling, and preventing kidney calculi. Ibn-Sina introduced very advanced drug designing based on drug delivery, targeting the organ, deposition in the site of action, pain control, wound healing, clearance after action, and supporting the organ. Using Ibn-Sina's ideas help scientists to choose better drugs with a historical background to reduce the cost of therapies and research projects.

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INTRODUCTION

Ibn-Sina (known as *Avicenna* in western literature), a Persian scientist, is regarded as the most famous and influential polymath of the Islamic Golden Age. Dante included Ibn-Sina with other influential scientists, such as Hippocrates and Galen, in his *Divine Comedy (Inferno Canto IV)*. Ibn-Sina was known as the *Prince of Physicians*, *Aristotle of Arabs*, *Galen of Islam*, and the *Second Master* (after Aristotle).¹ Ibn-Sina contributed to medicine, philosophy, astronomy, chemistry, geology, psychology, theology, mathematics, physics, and poetry. He wrote 450 treatises on a wide range of subjects; 40 of his books which concentrated on medicine survived. His most celebrated book in medicine is the *Canon of Medicine (Al-Qanun fi al-Tibb)*, translates as the rules of medicine). The *Canon of Medicine* is considered as one of the most famous medical books in history. The *Canon of Medicine* presents a clear and organized summary of all the medical knowledge of the time. The *Canon of Medicine* was translated into a number of languages, including Persian, Latin, Chinese, Hebrew, German, French, and English.²

The *Canon of Medicine* has been one of the main medical references for 100 years in Europe, Asia, and Africa. Sir William Osler described the *Canon of Medicine* as "the most famous medical textbook ever written" and "a medical bible for a longer time than any other work."³ The *Canon of Medicine* consists of the following 5 books: Book I, general anatomy and the principles of medicine; Book II, pharmacology; Book III, diseases of the special organs; Book IV, general medical conditions; and Book V, formulary. In Book III, each chapter begins with a brief account of anatomy followed by a list of signs and symptoms related to diseases of a specific organ.²

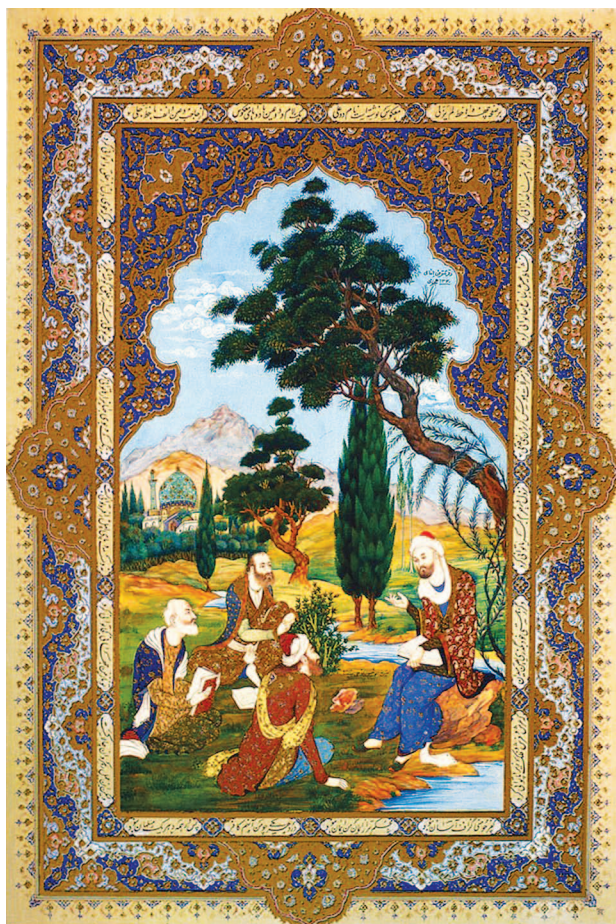
BIOGRAPHICAL SKETCH

Ibn-Sina was born to a Persian family on 23 August 980 AD in Afshaneh, near the city of Bokhara (in old Persia). Ibn-Sina's father, Abdullah, was a local governor, and his mother was Setareh. It was obvious since childhood that Ibn-Sina was clever. According to his autobiography, Ibn-Sina had memorized the Quran and important Persian writings by 10 years of age. He began to study

medicine and philosophy and became a well-known physician when he was just 18 years of age. When he treated the Prince of the Samanid dynasty (Nuh), Ibn-Sina was given permission to use the Royal Library as a reward. It was a great opportunity for Ibn-Sina to gain access to many important and unique books and complete his knowledge. After Mahmood Ghaznavi defeated the Samanid dynasty, Ibn-Sina went to Gorgan in northern Iran, where he began writing the *Canon of Medicine*. He also lived in other parts of Iran, such as Ray (near Tehran), Isfahan (central Iran), and Hamadan (western Iran). Ibn-Sina died from a recurrent abdominal ailment in June 1037 at 58 years of age and is buried in Hamadan (Figure).⁴

CONTRIBUTIONS TO KIDNEY CALCULI TREATMENT

The anatomy and physiology of the renal system were explained briefly in Book III, Section 18.



Avicenna and his pupils: contemporary miniature (Shiraz school) by Mirza Aqa Imam.

Ibn-Sina correctly pointed out that the kidney does not have sensory nerves internally, but sensory nerves are distributed on the surface of the kidney. One of the main approaches used by Ibn-Sina in the diagnosis of kidney diseases is based on a detailed examination of the urine.⁵ Ibn-Sina's idea on the methods for collecting and examinations of the characteristics of urine in healthy and sick individuals are similar to the methods described in the *Campbell Walsh's Text book of Urology*.⁶ Moreover, he described thirst, leg edema, oliguria, polyuria, dysuria, enuresis, retention, and hematuria as signs of kidney disease. Ibn-Sina described in detail urinary tract infections and abscess formation in the renal system, as well as obstruction, nephrolithiasis, small-sized kidneys, polycystic kidneys, and proteinuria (included as a type of edema with "foaming urine"). Ibn-Sina was the first to recommend the use of soft malleable catheters made of leather and silver. Ibn-Sina cautioned that catheters should have many holes, so that if one becomes plugged, medicine can be injected or urine drained out through the other holes, avoiding withdrawing and reinserting the catheter. Ibn-Sina was the first to point out the fact that hematuria might be due to causes outside the urinary system, for example, blood diseases.^{5,6}

Ibn-Sina introduced the kidney calculi section with his theories on the etiology of kidney calculi formation. He believed that kidney calculi were caused by coalescence of phlegmatic material, sticky mucus, pus, and rarely, bloody material around a dense core particle. Kidney calculi are usually associated with impaired function of the kidneys, obstruction, inflammation of the urethra or bladder, and excessive heat within the urinary tract. Ibn-Sina believed that a kidney calculus is usually a hereditary disease. Ibn-Sina suggests that heavy foodstuff, dairy products, sour fruit, unclear water, and dark juices could increase the risk of kidney calculi. Furthermore, he suggests that different types of calculi are available and have differences in color, shape, and solidity. Bladder calculi are less in common women than men as the bladder outlet is less tortuous, shorter, and wider. Ibn-Sina proposed that constipation could be a risk factor for kidney calculi.^{6,7}

Ibn-Sina used urinalysis for the diagnosis of kidney calculi. He described the urine of calculus formers, which might have many red or yellow

gravel deposits. The patient may pass blood with large or coarse calculi, but not with small and soft calculi. Dysuria is more common with small calculi, because the calculi may obstruct the opening of the bladder and the patient may urinate unconsciously, rub the tip of the penis, and urinate again because the bladder is irritated. Pain is worse when calculi are formed or during the passage of the calculi to the bladder, otherwise patients feel heaviness in the flanks. Overeating makes pain worse, and after defecation, the pain will be reduced. Ibn-Sina distinguished between kidney and bladder calculi, which had not been described by physicians previously. Ibn-Sina provided a perfect description of the differential diagnosis between colonic and renal pain.⁸

Ibn-Sina's treatment strategy for kidney calculi was elimination of materials with the potential to form calculi, breaking the calculi, and removing the gravel by urine. Moreover, Ibn-Sina used several kidney tonics, muscle relaxants to facilitate the passage of calculi, analgesics, and wound-healing medicines (Tables 1 to 3). To obtain the optimal treatment results, each formulary should have 6 actions, according to Ibn-Sina, as follows:

First, it must have dissolving and breaking effects on the calculus. Calculus dissolving and destructing drugs are categorized into 4 groups, as follows: (1) those acting on small and soft gravel; (2) those affect kidney calculi, but do not have suitable effects on bladder calculi, such as the *Jew's stone*; (3) those mainly affect kidney calculi and have some benefits on bladder calculi; and (4) those with dissolving effect on both kidney and bladder calculi, like *scorpion ash*.

Second, kidney calculus drugs should be directed to the calculi. Ibn-Sina introduced some herbal medicines, such as *black pepper*, *pennyroyal*, and *cinnamon*, as drug targeting agents for kidney calculi.

Third, some drugs are needed to maintain medicines at the site of action and concentrate in the kidney. These drugs usually have high viscosity and are sticky agents, like the gums of *polypody* and *Persian walnut*.

Fourth, strong diuretics are needed to pass gravel, which remain from calculus destruction.

Fifth, calculi usually cause some harm to the kidney. Thus, kidney tonic drugs, such as *spikenar*, *ginger*, *iris*, *centaurea*, *vitex*, *burra gokhru*, *pomegranate*, *camel grass*, *damask rose*, *sandalwood*, and *cassia*, are

used in these formulations.

Sixth, for pain control, Ibn-Sina advised giving sedatives during colic attacks and helped to move the calculi once the pain had subsided. These drugs included *opium*, *flax*, *Turkish pine*, *hazel*, and *marshmallow*.

Moreover, Ibn-Sina recommended that calisthenics, massage, hydrotherapy, dry and wet cupping, equitation, and climbing stairs are a beneficial method for passing gravel and small calculi. He observed that bathing in sulfur water penetrated the skin and was useful for local therapy of calculi. Ibn-Sina advised that lithotomy should be reserved for patients in whom the calculus cannot be dislodged by other means; he emphasized perineal urethrostomy. He also described surgery via the transperineal route and warned the surgeon of the proximity of the vasa deferentia, prostate gland, and neurovascular bundle and exposure in this position. It is interesting that he used grasping forceps for removal of the bladder calculus and emphasized on removing all calculus fragments. He explained a technique similar to the use of a Babcock forceps for prevention of calculus migration. Complications of calculus surgery and cystotomy are also addressed with scientific precision.^{9,10}

For prevention of the recurrent calculi, Ibn-Sina advised avoiding heavy food and drinks. He also advised to drink plenty of fluids and mild diuretics. He believed that vomiting could reduce materials which can change into calculi!

RESULTS AND DISCUSSIONS

In the *Canon of Medicine*, 65 herbal, 8 animal, and 4 mineral medicines are mentioned as beneficial drugs for destructing, expelling, and preventing kidney calculi (Tables 1 to 3). Of the 65 medicinal plants, 24 were terpenoid volatile oil-rich herbs. A placebo-controlled randomized trial shows terpene combinations such as Rowatinex, has calculi clearance, diuretic, and urinary tract anti-spasm effects.¹¹

Although there are no studies on most of the drugs introduced by Ibn-Sina, some investigations confirmed the potential of some of the drugs. The *in vivo* studies on rats have shown the following:

- *Caraway* has furosemide and thiazide-like activities¹¹;
- *Satavar* significantly reduces the level of

Table 1. Herbal Medicines Mentioned in the Canon of Medicine for Kidney Calculi

Scientific Name	Family	Part Used	English Name	Local Name	Action	Preparation
<i>Adiantum capillus-veneris</i> L	Adiantaceae	Whole plant	Southern maidenhair fern	Parsiavashan	Dissolves and expels stones	...
<i>Alisma plantago-aquatica</i> L	Alismataceae	Whole plant	Mad-dog weed	Mizmar raii	Useful in kidney stones	Decoction
<i>Carum carvi</i> L	Apiaceae	Fruit	Caraway	Komun	Dissolves and expels stones	With olive oil and the flour of broad bean
<i>Carum copticum</i> L	Apiaceae	Fruit	Ajowan	Nankhah	Dissolves and expels stones	...
<i>Foeniculum vulgare</i> Mill	Apiaceae	Fruit	Fennel	Razianeh	Dissolve stones	...
<i>Ferula persica</i> Willd	Apiaceae	Oleo gum resin	Galbanum	Sakbinaj	Dissolves stones	...
<i>Petroselinum crispum</i> (Mill) Fuss	Apiaceae	Whole plant	Parsley	Karats-e- Jebeli	Dissolves and expels stones	...
<i>Levisticum officinale</i> WDJKoch	Apiaceae	Fruit	Lovage	Kashem	Diuretic	...
<i>Peucedanum grande</i> CB Clarke	Apiaceae	Fruit	Wild carrot	Dughou	Diuretic	...
<i>Acorus calamus</i> L	Araceae	Root	Sweet Flag	Vaj	Diuretic	...
<i>Asparagus racemosus</i> Willd	Asparagaceae	Root	Satavar	Haliun	Dissolves and expels stones	...
<i>Scolopendrium vulgare</i> L	Aspleniaceae	Leaf	Hart's tongue fern	Saghuluqhandriun	Dissolves and expels stones	...
<i>Tanacetum parthenium</i> (L.) Sch Bip	Asteraceae	Flower	Feverfew	Aghhowan	Breaks bladder stones	With oxymel
<i>Matricaria chamomilla</i> L	Asteraceae	Flower	Camomile	Babooneh	Induces diuresis and expels stones	...
<i>Artemisia vulgaris</i> L	Asteraceae	Whole plant	Mugwort	Brenjiasf	Dissolves kidney stones	...
<i>Artemisia abrotanum</i> L	Asteraceae	Fruit	Southernwood	Qeysum	Dissolves kidney and bladder stone	...
<i>Aster tripolium</i> L	Asteraceae	Fruit	Sea Aster	Taraghiun	Dissolves bladder stone	...
<i>Artemisia absinthium</i> L	Asteraceae	Whole plant	Wormwood	Afsantin	Dissolves and expels stones	...
<i>Cynara scolymus</i> L	Asteraceae	Root	Artichoke	Horshof	Dissolves and expels stones	...
<i>Arnebia euchroma</i> L	Boraginaceae	Root	...	Abu Khalisa	Useful in kidney stones	Decoction with hydromel
<i>Brassica oleracea</i> L	Brassicaceae	Ash of Fruit	Wild cabbage	Kurunb	Dissolves stones	...
<i>Raphanus sativus</i> L	Brassicaceae	Fruit	Radish	Fojl	Dissolves and expels stones	...
<i>Commiphora mukul</i> Engl	Burseraceae	Gum	Guggal	muqul al-makki	Dissolves and expels stones	...
<i>Cannabis sativa</i> L	Cannabaceae	Fruit	Marijuana	Shahdanaaj	Dissolves and expels stones	...
<i>Gypsophila struthium</i> Willk	Caryophyllaceae	Root	Egyptian soapwort root	Kondos	Dissolves stones (very effective)	...
<i>Cucumis melo</i> L	Cucurbitaceae	Fruit	Muskmelon	Betteikh	Induces diuresis and removes small stones of kidney and bladder	...
<i>Bryonia alba</i> L	Cucurbitaceae	Stem	White Bryony	Fashara	Dissolves and expels stones	...
<i>Cyperus rotundus</i> L	Cyperaceae	Root and fruit	Nutgrass	Soad	Dissolves and expels stones	...
<i>Diospyros ebenum</i> Koenig	Ebenaceae	Wood	Ebony	Abnus	Dissolves kidney stones	...
<i>Cicer arietinum</i> L	Fabaceae	Fruit	Chickpea	Hemas	Dissolves and expels kidney and bladder stone	Decoction of black chickpea admixed with almond oil, radish, and celery
<i>Dolichos biflorus</i> L	Fabaceae	Fruit	Horse gram	Quit	Dissolves kidney and bladder stone	...
<i>Medicago sativa</i> L	Fabaceae	Roots	Alfalfa	Ratbah	Dissolves and expels stones	...
<i>Trigonella foenum-graecum</i> L	Fabaceae	Fruit	Fenugreek	Holbeh	Dissolves and expels stones	...
<i>Ocimum basilicum</i> L	Lamiaceae	Whole plant	Basil	Nammiim	Expels stones	...

Table 1. Continue

<i>Mentha pulegium</i> L	Lamiaceae	Whole plant	Pennyroyal	Foodanaj	Dissolves and expels stones	...
<i>Ajuga chamaepitys</i> Schrb	Lamiaceae	Whole plant	Yellow bugle	Kamafitius	Dissolves and expels stones	...
<i>Teucrium polium</i> L	Lamiaceae	Whole plant	Felty germander	Jaadeh	Dissolves and expels stones	...
<i>Teucrium scordium</i> L	Lamiaceae	Whole plant	Diascordium	Osghurdiun	Dissolves and expels stones	...
<i>Vitex agnus-castus</i> L	Lamiaceae	Fruit	Vitex	Banjangosht	Diuretic	...
<i>Laurus nobilis</i> L	Lauraceae	Bark of roots	Bay Laurel	Ghar	Dissolves and expels stones	...
<i>Cinnamomum aromaticum</i> Nees	Lauraceae	Bark	Cassia	Salikheh	Dissolves and expels stones	...
<i>Scilla indica</i> Roxb	Liliaceae	Bulb	Squill	Onsol	Dissolves and expels stones	In form of vinegar and oxymele
<i>Lawsonia inermis</i> L	Lythraceae	Roots	Henna	Hena	Dissolves and expels stones	...
<i>Alceae officinalis</i> L	Malvaceae	Root and fruit	Marshmallow	Khatmi	Dissolves and expels stones	Decoction
<i>Paeonia officinalis</i> L	Paeoniaceae	Fruit	Peony	Oud al-salib	Children renal stones	...
<i>Cedrus deodara</i> (Roxb) GDon	Pinaceae	Latex	Deodar	Diodar	Dissolves kidney and bladder stone	...
<i>Pinus eldarica</i> Medw	Pinaceae	Fruit	Turkish pine	Hab e Senowbar	Stops the formation of stones in bladder	...
<i>Piper cubeba</i> L	Piperaceae	Fruit	Cubeb	Kababeh	Facilitates the flow of sandy materials through the urine and expels kidney and bladder stones	...
<i>Piper nigrum</i> L	Piperaceae	Fruit	Black pepper	Felfel	Dissolves and expels stones	...
<i>Cymbopogon schoenanthus</i> Spreng	Poaceae	Inflorescence	Camel grass	Izkhar	Dissolves and expels stones	...
<i>Cynodon dactylon</i> (L) Pers	Poaceae	Whole plant	Bermuda Grass	Najm	Dissolves and expels stones	Decoction
<i>Rumex acetosella</i> L	Polygonaceae	Root	sheep's sorrel	Hommaz	Dissolves kidney and bladder stone	With wine
<i>Polygonum aviculare</i> L	Polygonaceae	Whole plant	Common Knotgrass	Asa- Arraii	Dissolves and expels stones	...
<i>Nigella sativa</i> L	Ranunculaceae	Fruit	Black seed	Shuniz	Useful in kidney and bladder stone	...
<i>Amygdalus communis var amara</i> L	Rosaceae	Fruit (oil)	Almond	Lauz	Dissolves stones	Bitter almond oil with iris
<i>Prunus virginiana</i> L	Rosaceae	Fruit	Chokecherry	Mihlab	Useful in kidney and bladder stone	...
<i>Rubus fruticosus</i> L	Rosaceae	Fruit, flower and roots	Blackberry	Ullaiq	Dissolves and expels stones	...
<i>Prunus cerasus</i> L	Rosaceae	Fruit, stalk	Sour cherry	Gharsia	Dissolves and expels stones	...
<i>Crataegus azarolus</i> L	Rosaceae	Oleogum resin and fruit	Azarole	Zaaroor	Dissolves and expels stones	...
<i>Potentilla reptans</i> L	Rosaceae	Root	Cinquefoil	Bantafelone	Dissolves and expels stones	...
<i>Valeriana wallichii</i> DC	Valerianaceae	Root	Indian Valerian	Mow	Diuretic	...
<i>Vitis vinifera</i> L	Vitaceae	Gum	Grape	Karm	Dissolves stones	...
<i>Costus arabicus</i> L	Zingiberaceae	Oil of roots	...	Qhost	Dissolves and expels stones	...
<i>Tribulus terrestris</i> L	Zygophyllaceae	Fruit and roots	Burra gokhru	Hasak	Dissolves and expels kidney and bladder stone	...
<i>Peganum harmala</i> L	Zygophyllaceae	Fruit	Harmal	Sodab barri	Dissolves and expels stones	...

Table 2. Animal-origin Medicines Mentioned in the *Canon of Medicine* for Kidney Calculi

English Name	Part Used	Local Name	Action	Preparation
Onager	Urine	Goor-e-khar	Dissolves bladder stone	...
Lumbricus	Whole	Kharatin	Induces diuresis and expels stones	With frankincense
Mouse	Stool	Moush	Dissolves kidney stones	Ash and oil
Scorpiones	Whole	Aqrab	Dissolves and expels stones (very effective)	Ash
Rabbit	Whole	Arnab	Dissolves and expels stones	Ash
Hen	Eggshell and feces	Bayz	Dissolves and expels stones	Ash
Pigeon	Feces	Hamman	Dissolves and expels stones	Smoke to urinary tract
Hedgehog	Spines	Ghonfoz	Expels stones	With frankincense

Table 3. Mineral Medicines Mentioned in the *Canon of Medicine* for Kidney Calculi

English Name	Local Name	Action	Preparation
Sponge	Esfanj	Dissolves and expels kidney and bladder stones	...
Jews stone	Hajar al-yahud	Dissolves and expels kidney and bladder stones	...
Glass	Zujaj	Dissolves and expels kidney and bladder stones	Powdered and burnt
Natron	Buragh	Dissolves and expels stones	...

calcium, oxalate, and phosphate, and elevates the concentration of magnesium¹²;

- *Radish* inhibits the formation of and decreases the weight of calculi, and increases the volume of 24-hour urine collections¹³;
- *Fenugreek, black seed ethanolic, and Bermuda grass* extracts reduce levels of calcium oxalate deposition¹⁴⁻¹⁶;
- Turkish pine aqueous extract prevents calcium oxalate deposition without producing diuresis¹⁷; and
- *Burra gokhru* ethanolic extract shows a significant dose-dependent protection against urolithiasis induced by glass bead implantation.¹⁸

Muskmelon significantly increases urine volume by increasing the glomerular filtration rate and decreasing tubular re-absorption in dogs.¹⁹ *Lovage*, which is approved by the German Commission E, is a strong diuretic for use in urinary gravel.²⁰

Some drugs, such as Jew's stone, have been used for centuries in both western and eastern countries.^{19,21-23} Recently, Jew's stone has been used as one of the Cystone components, which is beneficial for kidney calculi as confirmed by randomized clinical trials.²⁴ However, there is no information about the chemical composition, pharmacologic, and toxicologic effects of Jew's stone. Using a specific drug for a specific disease in different cultures raises the potential for positive results in further studies.

COMMENTS

The ideas of Ibn-Sina on the causes of kidney

calculi in some cases, such as dairy products, are similar to what we now know. His surgical methods were advanced for his time.⁹ He introduced very advanced drug design based on drug delivery and targeting organs, deposition on the site of action, pain control, wound healing, clearance after action, and support of the organ. However, the accuracy of his ideas is not examined, but his advanced theories are valuable and may be one of the first theories in drug targeting and delivery. His idea about using topical drugs for urolithiasis is interesting. He used medicinal smoke directed to the urinary tract for expelling calculi. This method is used in other traditional medicines for drug delivery to urinary tract.²⁵ Kidney calculi have been problematic for humans for thousands of years. The side effects and costs of surgery and extracorporeal shock-wave lithotripsy have resulted in enormous research efforts to find medicinal therapies.²⁶ Investigations on herbal drugs, which have a historical background, usually lead to interesting results. In this work, we have introduced one of the brilliant figures in the medieval age of medicine and identified the scientific name of natural medicines which was used for kidney calculi. It would be prudent for researchers to review most of the historical books because Ibn-Sina collected the medical knowledge of his time and physicians used his *Canon of Medicine* as a trustworthy reference.

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CONFLICT OF INTEREST

None declared.

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