USING SULFUR-CONTAINING MINERALS IN MEDICINE:
IRANIAN TRADITIONAL DOCUMENTS AND MODERN
PHARMACEUTICAL TERMINOLOGY

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ABSTRACT

Sulfur occurs naturally in the earth’s crust as a pure element (native sulfur), as well as sulfide and sulfate minerals. From the biochemical point of view, sulfur is a vital element because it is a constituent of enzymes and other key proteins. In addition to modern uses of minerals, in old Iranian documents of traditional medicine, attention was paid to physico-chemical properties of minerals and the various methods of administration. In this review, the traditional usage of sulfur and sulfide minerals (e.g. orpiment, realgar and stibnite) and sulfate minerals (e.g. alum, jarosite, epsomite and melanterite) as documented in the Canon of Medicine of Avicenna (also known as Ibn Sina) and the Zakhireh Khazarmshahi of Jorjani, is compared with new findings about the advantages and disadvantages of these minerals in medical geology.

The main conditions for the selection of mineral drugs was described first by Avicenna. There is a high correlation between old and modern pharmaceutical practices. The most important results concern the application of alum as a hemostatic agent (to inhibit hemorrhages), the use of jarosite as a method for treating osteoarthritis, the choice of melanterite for treating eczema, killing insects and as an anti-bacterial agent, the use of epsomite as an active ingredient in laxatives, homeostatics and mineral supplements, and the extensive use of sulfur in dermatology for its keratolytic effects and its supposed antimicrobial effects. In this review, newly developed pharmaceutical information about the use and effects on health of sulfide minerals will be compared to traditional pharmaceutical applications.

Keywords: sulfur, alum, traditional medicine, modern pharmacy, sulfide and sulfate minerals, medical geology, Iranian traditional pharmacies
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1. INTRODUCTION

The use of plants, herbs, minerals, gems and soils to cure ailments goes back to before recorded history, most prominently in ancient Iran, India, Egypt and China. The development of ancient pharmacopeias and the recognition of the efficacy of different materials in medicine have resulted from cumulative human experiences. Today, modern technology plays an increasingly important role in medicine. Researchers can obtain detailed knowledge so that recent studies can confirm previous data, or alternatively refute the findings of earlier studies. This paper focuses on ancient Iranian medicine, and in particular on the Canon of Medicine of Avicenna (also known as Abou Ali Ibn Sina). This encyclopedia of medicine, in five books, was completed in 414 A.H. (1023 A.D.) by Avicenna who died of colic in 428 A.H. (1037 A.D.) (Nasser et al. 2009; Saffari and Pakpour 2012).

The first book of the Canon comprises essays on basic medical and physiological principles, anatomy, regimen and general therapeutic procedures. The second book contains a list of medical substances, arranged alphabetically, followed by an essay on their general properties. The diagnosis and treatment of diseases specific to one part of the body, and diagnosis and treatment of conditions covering multiple parts of body or the entire body, are discussed in the third and fourth volumes of the Canon, respectively. Finally, the formulation of compound remedies is presented in the last volume of the Canon (Nasser et al. 2009).

In the Canon, Avicenna made interesting remarks about inorganic chemistry that pertain to the subject of this study. In particular, he discussed the applications of sulfur-bearing minerals in
medicine. The drug classification used by Avicenna is entirely consistent with new approaches such as those used by the World Health Organization (WHO 2003).

To understand how the terms and concepts of ancient Iranian pharmaceuticals were used in the Canon were applied, the Persian medical encyclopedia, Zakhiireh Kharazmshahi, by Jorjani (504 A.H.; 1110 A.D.) is utilized (see Figure 1). Seyed Esmaeel Jorjani (1041–1136, also known as Jorjani), is one of the most famous Iranian physicians and he used Avicenna’s Canon and referred to it as one of the most important sources for his encyclopedia.

2. SULFUR

Sulfur is a constituent of enzymes as well as some biologically key proteins. For example, methionine and cysteine are considered to be the principal sulfur-containing amino acids and they play critical roles in cell metabolism. According to the Canon of Avicenna the materials around us have some combination of four characteristics that are: ‘hotness’, ‘coldness’, ‘dryness’ and ‘wetness’. In the case of sulfur, it is a ‘hot’ and ‘dry’ matter. Avicenna said:

Sulfur water treats nerves; relieves distension and spasm pains; cleanses the skin from pustules, chronic bad sores, roughness, freckles, leukoderma and vitiligo. However, it weakens the stomach and appetite (Sina 1989, p.175; Jorjani 2011, pp. 118–120).

Mineral water was a main source of sulfur in traditional medicine. Mineral water that contained sulfur was a useful treatment for leukoderma\(^1\) and vitiligo\(^2\) and nowadays, sulfur is known as a mild antiseptic and disinfectant. Sulfur has an inhibiting effect on various types of bacteria, including Propionibacterium acnes growth as well as Sarcoptes scabiei, some Streptococci, and Staphylococcus aureus. This anti-bacterial activity purportedly results from the

1. Leukoderma is a cosmetic problem that identified with localized loss of pigmentation of the skin.
2. Vitiligo is a disease in which the pigment cells of the skin, melanocytes, are destroyed in certain areas.
inactivation of sulphydryl groups contained in bacterial enzyme systems (Gupta and Nicol 2004; Sanfilippo and English 2006). In addition, sulfur is a constituent of enzymes as well as some biologically key proteins. For example, methionine and cysteine are considered to be the principal sulfur-containing amino acids and they play critical roles in cell metabolism.

Not all water containing sulfur is beneficial, however. Avicenna (Sina 1989, p. 176) alluded to the toxic effects of water containing sulfur and this matter is confirmed by modern environmental and medical research.

It is also an effective keratolytic reducer. Sulfur has been used in dermatology because of its keratolytic effects and also its supposed anti-microbial effects. The keratolytic effect of sulfur is probably due to the reaction between sulfur and the cysteine in keratinocytes, thereby forming hydrogen sulfide. Hydrogen sulfide can break down keratin, and thereby result in the keratolytic activity of sulfur (Carretero and Pozo 2010).

Avicenna (Sina 1989, p. 174) considered sulfur as a nerve treatment; and in modern pharmacy, for example, there are sulfurzyme drugs, which are outstanding sources of organic sulfur, that equalizes water pressure inside the cells and reduces pain. Sulfurzyme works well to repair damage not only to the nerves but also to the myelin sheath around the nerves. When fluid pressure inside cells is higher than outside, pain is experienced. Sulfurzyme has the ability to equalize fluid pressure inside and outside the cells by modifying the protein envelope that surrounds the cell, so that water transfers freely in and out (De Monte 2012). However, to be effective, sulfur requires the presence of calcium and vitamins B and C so that the body can metabolize it.

Sulfur has been applied traditionally as lotions, ointments, and creams for acne treatment. However, nowadays, sulfur minerals are applied externally in the form of shampoo, suspensions, lotions, ointments and creams and sulfur is not absorbed in large quantities. As Carretero and Pozo (2010) mentioned, only about 1% of topically applied sulfur is systemically absorbed. Adverse effects from topically applied sulfur are uncommon and are mainly limited to the skin (Lin et al. 1988). The uses of sulfur in traditional and modern medicine are presented in Table 1.

<table>
<thead>
<tr>
<th>Traditional uses</th>
<th>Modern applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning the skin from pustules</td>
<td>Anti-microbial and anti-acne creams &amp; emulsions</td>
</tr>
<tr>
<td>Keratolytic reducers</td>
<td>Sulfur creams</td>
</tr>
<tr>
<td>Treatment of neuralgia and spasm pain</td>
<td>Sulfurzyme drugs (capsule, powder, supplement)</td>
</tr>
</tbody>
</table>

3. SULFATE MINERALS

Avicenna (Sina 1989, p. 294) pointed out that different forms of alum (or zaj) have various colors. He said that most of these varieties are soluble substances (Sina 1989, p. 294). Those that are in the form of stones are not soluble, but those substances that are composed of vitriol are soluble. In some cases, alum occurs in liquid form but these liquids generally become condensed and solid over time. According to Avicenna (Sina 1989, p. 294) qalqatar is yellow zaj (also known as jarosite). Qalqadis is white zaj (also known as alunite), qalqand is green zaj (also known as melanterite), and Siryan is red zaj (also known as epsomite). All these kinds of alum are ‘hot and dry in the second degree’ according to his classification. They are caustic, produce dandruff and are astringent. White zaj is the most astringent while the yellow variety is moderately so. Yellow zaj, in turn, is more astringent than the green variety. The scientific names of different alum minerals and their terms and meaning in Persian and traditional documents are represented in Table 2.

3. Sulphydryl groups are functional group consisting of a sulfur bonded to a hydrogen atom.
4. Keratolyt is a skin problem in which the epidermis produces excess skin such as warts or calluses.
5. Keratinocyte is the predominant cell type in the epidermis, the outermost layer of the skin, constituting 90% of the cells found there.
Table 2. Persian and traditional terms used for some sulfur mineral groups

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Persian name</th>
<th>Traditional term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alunite</td>
<td>Zaj (white)</td>
<td>Qalqadis</td>
</tr>
<tr>
<td>Jarosite</td>
<td>Zaj (yellow)</td>
<td>Qalqatar</td>
</tr>
<tr>
<td>Melanterite</td>
<td>Zaj (green)</td>
<td>Qalqand</td>
</tr>
<tr>
<td>Epsomite</td>
<td>Zaj (red)</td>
<td>Siryan zaj</td>
</tr>
</tbody>
</table>

Alum is a generic term for hydrated sulfates of aluminum (or other trivalent cations) and an alkali cation (or comparable monovalent cation). Jarosite, melanterite and epsomite are different hydrated sulfate minerals. In old documents, such as the Canon, those are in a unique category and their various applications in traditional medicine have been reported. According to the Canon (Sina 1989, p. 294), the best kind of zaj come from Egypt (red zaj) and Cyprus (green zaj), however good quality white and yellow zaj is found in Iran, especially in the northwest (Azarbaijan).

Avicenna (Sina 1989, p. 135) said that alum is an effective drug for treatment of itching, lice, ozostomia, and stench of the armpit. Nowadays alum (= white zaj) is widely used as a deodorant because of its high astringency. Also, alum (in 1–4% solutions) is used in mouthwashes and in solid form (powder) for stomatitis and pharyngitis (Carretero and Pozo 2010). Alum can be put on canker as a topical treatment. It causes a burning sensation, and will cause the mouth to pucker, but it will relieve the pain and help the sore clear up quickly. It is recommended that the canker and mouth are rinsed with water after a few minutes. This form of topical treatment should be repeated once or twice a day, as needed. The functional performance of sulfur in reducing the inflammation is shown in Figure 2.

In the Canon, Avicenna wrote:

Alum has the potency of resistance and desiccation and stops all kinds of bleeding and flow of superfluous matters towards an organ and yellow zaj stops uterine hemorrhage. . . Alum and ferric sulfate waters are beneficial for menorrhagia, anal bleeding (hematochezia), stomach sensitivity, idiopathic recurrent miscarriage, puffiness and excessive sweating. (Sina 1989, pp. 172, 367).

In modern pharmaceutical practice, alum is also applied as a homeostatic agent (to inhibit hemorrhages) for cuts or superficial skin damage. It is a suggested treatment for anterior nasal bleeding, and is applied by packing with a ribbon gauze soaked with 1% alum. Alum acts as an astringent leading to protein precipitation on the irritated surface. A 1% solution is used diluted in sterile distilled water. As its pH is 4.5, salts precipitate if pH is neutralized. As a result, alum cannot be combined with local anaesthesia, as the anaesthesia is rendered useless. The haemostatic packing should be kept in the site until bleeding is controlled (usually a few days). If no commercial preparations are available locally, then gauze soaked in 1% alum can be used (Hulme and Wilcox 2008). According to Paes et al. (1986), a single case study described a 71-year old man with rectal carcinoma and uncontrolled bleeding. Gauze soaked in a 1% solution of alum was packed into the rectum under general anaesthesia and left in situ for three days. The procedure was repeated and the patient remained free from bleeding for at least three months. Side effects of alum treatment

6. Bad breath.
7. An inflamed and sore mouth that can disrupt a person's ability to eat, talk, and sleep.
8. An infection or irritation of the pharynx or tonsils.
include vesical tenesmus\(^9\) and spasms and suprapubic pain. These can be effectively managed with anti-spasmodic drugs (Hulme and Wilcox 2008).

Avicenna believed that alum had many uses. For example, he claimed that all kinds of zaj were useful in the treatment of wet scabies and favus (Sina 1989, p. 294). He also believed that qalqand (melanterite) can remove the harmful effects of fungus. Furthermore, Avicenna argued emphatically for the antiseptic and antibacterial effects of qalqand (Sina 1989, p. 294). In the Canon of Avicenna, he noted that green alum remediates the ear tick and ear mites, and he stated that:

green vitriol is hot and dry up to the fourth degree. It is a desiccant and hardener. It blocks pores of the body with adverse effects. It is corrosive and somewhat astringent and burning. It is also useful in sinusitis. It stops epistaxis. When infused into the nose it ‘cleanses’ the head. In short, it is one of the cleansing drugs for the ear affected with ‘cold’ pain. Besides it kills the ear worms. It removes the harmful effects of fungus. (Sina 1989, p. 294).

Today, the pharmacological effects, function and chemical components of melanterite are known and it is used to treat eczema, to kill insects, and to be used as an anti-bacterial agent (Shen 2014). Inorganic anti-bacterial minerals were considered by Shen (2014) on his patent report. The pharmacological effects of these minerals are shown in Table 3. Melanterite also is widely used as an anti-anemic because this mineral is highly soluble in water and contains Fe\(^{2+}\) ions in its structure (Carretero and Pozo 2010).

Avicenna said, quoting Galen, that qalqadis (alunite) would be altered to qalqatar (jarosite) (Sina 1989, p. 295). Brophy et al. (1962), implied that alunite \([\text{KAl}_3(\text{SO}_4)_2(\text{OH})_6]\) and jarosite \([\text{KFe}_3(\text{SO}_4)_2(\text{OH})_6]\) may form a solid solution series in nature. Alunite and jarosite are co-existing minerals that occur in alteration zones. In addition to all the medical uses of alum described above, Avicenna also noted that qalqatar can be useful for erysipelas\(^{10}\) treatment. He said that qalqatar is hot and dry in the third degree, it is a highly caustic drug. It stops haemorrhages and causes dryness. Its burnt form is more desiccant but less irritant. It is very astringent. When painted along with coriander juice, it is useful in herpes and erysipelas. It is used as a dusting powder on creeping and malignant ulcers. It erodes excessive flesh and absorbs the slough. It is useful in epistaxis and inflammatory conditions of the gums and eustachian tube, its collyrium proves to be useful for cleaning the eyes and softening swollen eyelids (Sina 1989, p. 294).

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Pharmacological effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanterite</td>
<td>Treats eczema, kills insects and anti-bacterial</td>
</tr>
<tr>
<td>Realgar</td>
<td>Detoxification, removes moisture, kills insects, anti-bacterial</td>
</tr>
<tr>
<td>Alum</td>
<td>Detoxification, kills insects, dries moisture, stops itch, wide spectrum anti-bacterial</td>
</tr>
<tr>
<td>Sulfur</td>
<td>Kills insects, stops itch, scabies, eczema, anti-bacterial</td>
</tr>
</tbody>
</table>

About red alum, Avicenna believed that it can be useful to fix loose teeth (Sina 1989, p. 483). In modern pharmaceutical practices, epsom salts have a vast range of applications. For example, they are used as a firming agent. According to a review by Carretero and Pozo (2010), epsomite commonly serves as the active ingredient in laxatives, homeostatics and mineral supplements.

The various medical uses, and related biological functions of alum, jarosite, epsomite and melanterite are presented in Table 4.

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9. The feeling of incomplete emptying of the bladder.
10. It is an infection of the upper dermis and superficial lymph.
Table 4. The use of alum and its family of sulfate minerals in traditional and modern pharmaceutical practices.

<table>
<thead>
<tr>
<th>Traditional uses</th>
<th>Modern use</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alum (in general):</strong></td>
<td>Pesticide shampoos</td>
<td>Antiseptic and disinfectant</td>
</tr>
<tr>
<td>Treatment for lice</td>
<td>Deodorant</td>
<td>High astringent capacity</td>
</tr>
<tr>
<td>Treatment for armpit stench</td>
<td>Haemostatic packing</td>
<td>Decrease capillary permeability; contraction of intercellular space</td>
</tr>
<tr>
<td>Anti-hemorrhage agent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomatitis and oral ulcers treatment</td>
<td>Colutorios (mouthwash)</td>
<td>Remove the moisture from the ulcer</td>
</tr>
</tbody>
</table>

**Melanerite:**
- Antiseptic and anti-bacterial agent
- There is no clear use mentioned in the Canon

**Jarosite:**
- Erysipelas treatment
- There is no clear use mentioned in modern pharmacological documents

**Epsomite:**
- Fix loose teeth
- Osmotic oral laxatives
- There is no clear use mentioned in the Canon

**Bathroom salts:**
- Flotation tank
- High water solubility; release Mg$^{2+}$

4. SULFIDE MINERALS

Avicenna implied that the water which flows from areas with arsenic mineralization can have many adverse effects on health (Sina 1989, p. 186). He mentioned two arsenic minerals: yellow and red zarnikh, which are orpiment and realgar, respectively. Avicenna emphasized the health threats of using these minerals in this paragraph from the Canon:

*Zarnikh leaves deep ulcers in the intestines and abdomen. Drinking zarnikh contaminated water and breathing it causes severe coughing, also stomach pain occurs and it causes interrupted urine and blood in faeces. Around the nails cooled, the person faints and tongue and throat become dry.* (Sina 1989, p. 136)

Ingestion of drinking water polluted by arsenic has been associated with a variety of skin lesions, which include increased or decreased pigmentation and keratosis. Blackfoot disease (or gangrene) also has been reported. The carcinogenic role of arsenic exposure is the increased risk of different kinds of cancer such as cancer of the skin, lung, liver, bladder, and kidneys (Selinus 2005).

In traditional medicines, small amounts of arsenic are used for therapeutic purposes, mainly in the form of arsenic minerals such as orpiment ($\text{As}_2\text{S}_3$), realgar ($\text{As}_4\text{S}_4$), and arsenolite (contains arsenic trioxide, $\text{As}_2\text{O}_3$). According to old documents, the nature of *zarnikh* (that is, realgar and orpiment) is ‘hot and dry’. Avicenna said

Orpiment is a disinfecting agent and it is an acrid matter. Realgar mixed with tallow and grease remedies gary or scab, it can eradicate lice. Orpiment and realgar treat the mouth and nose ulcer. Those are used in bronchitis pills (Sina 1989, p. 137).
He emphasized that its fumes are toxic. However according to the *Canon*, a pure sample of *zarnikh* which powders easily and smells of sulfur, is the best. Therefore, Armenian and Azerbaijani *zarnikh* and realgar were used by Avicenna (Sina 1989, p. 137). Realgar also was used for nails vitiligo by Avicenna. He also described the process of preparing *zarnikh* pills which is mentioned by Jorjani:

A ratl\(^{11}\) of orpiment, a ratl of realgar, 2 ratl lime, 8 awqiyah, 12 of burnt papyrus and 8 awqiyah acacia, all milled and mixed with milk and then pills are made. (Jorjani 2011, p. 750).

He also administrated realgar, alum, lime and ammonium chloride as anti-inflammation suppositories for nasal sinuses. *Zarnikh* with lime was traditionally used as depilatory powder. *Zarnikh* and lime, with or without borax, also were used to eradicate the purulent wen\(^{13}\) and abscess (Jorjani 2011, p. 726).

Pharmacological studies show that arsenic trioxide and realgar are effective against certain malignancies (Liu et al. 2009). Arsenic-bearing minerals, such as orpiment and realgar, were used externally for various skin diseases. Realgar as an ingredient was used in traditional oral remedies because of its antipyretic,\(^{14}\) anti-inflammatory, anti-ulcer, anti-convulsive and anti-schistosomiasis actions (Liu et al. 2009).

In modern medicine, as Panda and Hazra (2012) explain, inorganic arsenic is now accepted as a first line chemo-therapeutic agent against certain hematopoietic\(^{15}\) cancers. Orpiment and realgar are poorly absorbed in the gastrointestinal tract due to their low solubility, while the bioavailability of arsenic trioxide is similar to inorganic arsenic salts.

Depending on the absorbed dose, overt acute clinical findings range from moderate gastroenteritis to fatal cardiovascular collapse. There are no reports of attempted self-harm by intentional orpiment ingestion in the modern medical toxicology literature (Buchan et al. 2012). However, according to toxicological studies, a major concern for arsenic trioxide concerns the known cardiovascular toxicity. Also, gastrointestinal and dermal adverse effects may occur after prolonged use of arsenic minerals (Liu et al. 2009). However, arsenic speciation, bioavailability, and toxicity/benefit should be considered when evaluating the efficacy of arsenic-bearing minerals in traditional medicines.

Stibnite, which was called *ithmid* in the *Canon* of Avicenna, has been used with alum or lime for treatment of some skin diseases. Avicenna said:

*Ithmid* is highly brittle and it is cold in the first and dry in the second degree. It is astringent and desiccant without being irritant. It is useful for ulcers, heals them and removes excessive flesh. When applied with fresh fat, it does not ulcerate a burnt part of the body. If that part is already ulcerated, its application with wax and white lead, heals the affected part. It protects the eyes and removes the filth from their ulcers. Burnt lead is its substitute. (Sina 1989, pp. 65).

In modern pharmaceutical practice, for example, Candidol and Canker are two dermatological drugs which have been classified by WHO (2016) and their ingredients included sulfur and its components, such as sulfur iodide, are applied as ingredients in these two drugs.

5. CONCLUSIONS

In this essay, we have attempted to give a brief account of some of the mineral-based drugs which were used by Avicenna (about 1000 years ago) and their high compatibility with modern medical

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11. A ratl is a widespread traditional Islamic unit of mass. Almost always, 100 ratl = 1 quintar or a little less than a pound.
12. An awqiyah is 1/12 of ratl.
13. Suppurative and septic swelling in the skin
14. Antipyretic effect is reducing the fever or quelling it.
15. Hematopoietic cancers are relevant to all the other blood cells through the process of haematopoiesis. They are derived from mesoderm and located in the red bone marrow.
documents. In this effort, we used information from another traditional book, the Zakhireh Kharazmshahi, which was the most authoritative Persian medical book that achieved a clear understanding of the Canon of Avicenna. This positive correlation between traditional and modern medicine and pharmaceutical practices which are shown in this review, demonstrates that the knowledge of the ancients can be an effective method to demystify the field of traditional medicine. Nowadays, there are some serious mistakes made in the use of minerals in traditional medicine because of the incorrect identification of minerals as they were classified in ancient documents. Therefore, investigations of the main traditional books are needed to assure the correct identification of drug ingredients. Inadequate translations of old documents may cause problems when using minerals in traditional medical practices.

Sulfur is a vital element in metabolic reactions, hence it is used in different components of pharmaceutical products. In traditional medicine, there are many documents and papers describing its use and the minerals from which it is derived. In these references, early names, especially of minerals, are not always correctly correlated to new terms. Therefore, this article tries to extract the terms used in the Canon with the help of other, and earlier, authorities, and to correlate them to modern terminology.

REFERENCES


