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Mineralogical characterization of the traditional geopharmaceutical *ithmid* by XRF and XRD

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Abstract

Geopharmaceuticals, specifically minerals were used to treat various diseases from antiquity. *Ithmid* or kohl stone is one of the most-applied geopharmaceuticals in the Middle East, Africa, and South Asia. The usage of *ithmid* for eye make-up caused many concerns about the possible toxicity and lead poisoning, because the concentration of lead content is usually higher than the international standard limit. The goal of this study was mineralogical investigation of *ithmid* stones (three samples) from Iran using XRD and XRF. Also, traditional applications of *ithmid* were extracted and reported. X-ray diffractometer and X-ray fluorescence analysis was used to determine the composition of three samples of *ithmid* stone from Tehran, Shiraz, and Kerman. The indications suggested for *ithmid* in Traditional Iranian Medicine were extracted from *Makhzan al advieh*, *Qarabadin Salehi*, and *Qarabadin Kabir*. Major phase of *ithmid* samples were galena (PbS), and the main element was lead with a high concentration in all three samples. Based on traditional books, *ithmid* was used for ocular injuries, infectious wounds, and visual disorders. It was proved that *ithmid* has antimicrobial effects against pathogens involved in ocular infections, but regular application of such products is a potential threat for costumer health. Therefore, regular check-out of kohl products by authorities is necessary to avoid the risk of lead toxicity and resultant health issues.

Keywords: Geopharmaceutical, *Ithmid*, Kohl, Galena, XRD, XRF.

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1. Introduction

Medical geology, the study of the effect of geopharmaceuticals like minerals, gemstones, metalloids, and soils has a long background in health issues. Geological materials were well-known by Chinese, Indian, Arabic, Roman, and other ancient cultures (1). *Ithmid* (kohl stone or surma) is one of the famous geopharmaceuticals that is widely applied in the Middle East, Africa, and South Asia. Besides its cosmetic applications, specifically for eye make-up, *ithmid* has numerous therapeutic effects (2).

The elemental composition of *ithmid* samples available in local markets were investigated in various countries, such as Egypt, Tunisia, United

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Arab Emirates, Saudi Arabia, Iran and Oman. The content was analyzed basically by techniques such as X-ray diffraction (XRD) and atomic absorption spectrophotometery. The main components of *ithmid* was identified to be galena (PbS), amorphous carbon, zincite (ZnO), calcite ($CaCO_3$), elemental silicon, talc ($Mg_3Si_4O_{10}$(OH), cuprite (Cu_{20}), goethite (FeO(OH)), magnetite (Fe_3O_4 and barite ($BaSO_4$), cadmium, nickel, and chrome (3-7)

Application of *ithmid* is a matter of a great health concern, because the concentration of lead content in all samples is higher than the limit of the international standards (8). Lead enters the body through respiratory, gastrointestinal, perinatal (mother-to-fetus) and skin routes, but the most important and common route of lead contact is gastrointestinal and inhalation. Blood lead level is the important indicator for its toxic effects. Half-life of lead in adult men is 30 to 40 days, while it can be longer in children and pregnant women (9). Lead spreads into the soft tissues like liver, kidneys, brain, and bone marrow and it can remain for several months. Lead toxicity is the result of binding to sulfhydryl group of proteins, interfering with multiple enzyme systems such as cytochrome P_{450} enzymes, vitamin D synthesis and heme production. Moreover, lead causes some defects in calcium-dependent cellular functions. Lead is normally deposited in bone for more than 20 years (10).

Lead-containing traditional remedies can result in increasing blood lead levels, and lead poisoning. Following the application of such medicines by infants and children, lead encephalopathy may happen. Compared with adults, children are more susceptible to lead intoxication. Due to the rapid growth of the brain and high demand for nutrients, nervous system is more vulnerable for children under the age of six. Lead impairs learning, growth and development of nervous system in children, also it reduces memory and intelligence quotient (11).

Majority of researches in this field was focused on evaluation of *ithmid*-containing products, so, limited works are conducted on the stone. The aim of this study was mineralogical investigation of *ithmid* stones from Iran using XRD and XRF. An overview on traditional applications of *ithmid* was also provided.

2. Materail and Methods

2.1. XRD and XRF analysis

Three samples of *ithmid* (Figure 1) were purchased from the local market of Tehran (S_T), Kerman (S_K), and Shiraz (S_{SH}). They were deposited with the Voucher Nr. PM1300, PM1302, and PM1298 in Traditional Pharmacy department, Faculty of Pharmacy, Shiraz University of Medical Sciences. The samples were kept in a plastic bag in a cool and dry place away from sunlight and fumes before analysis procedures that were conducted in Mashhad analytical Geology Lab East Amethyst. The stones were ground to fine powders and then they were mounted in sample cups. To identify the composition of *ithmid*, each sample was subjected to X-ray studies employing Philips PW 1480 XRF spectrometer (UniQuant-software) linked to X40 software and minerals database. In XRF spectrometer, X-rays were generated in an

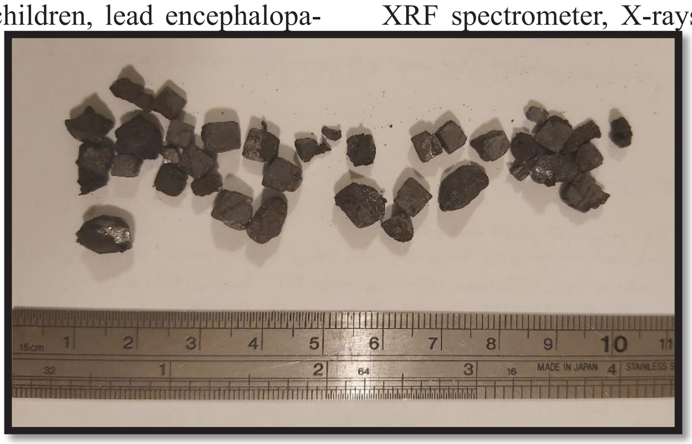

Figure 1. A sample of *ithmid* stone purchased from Shiraz, Iran.

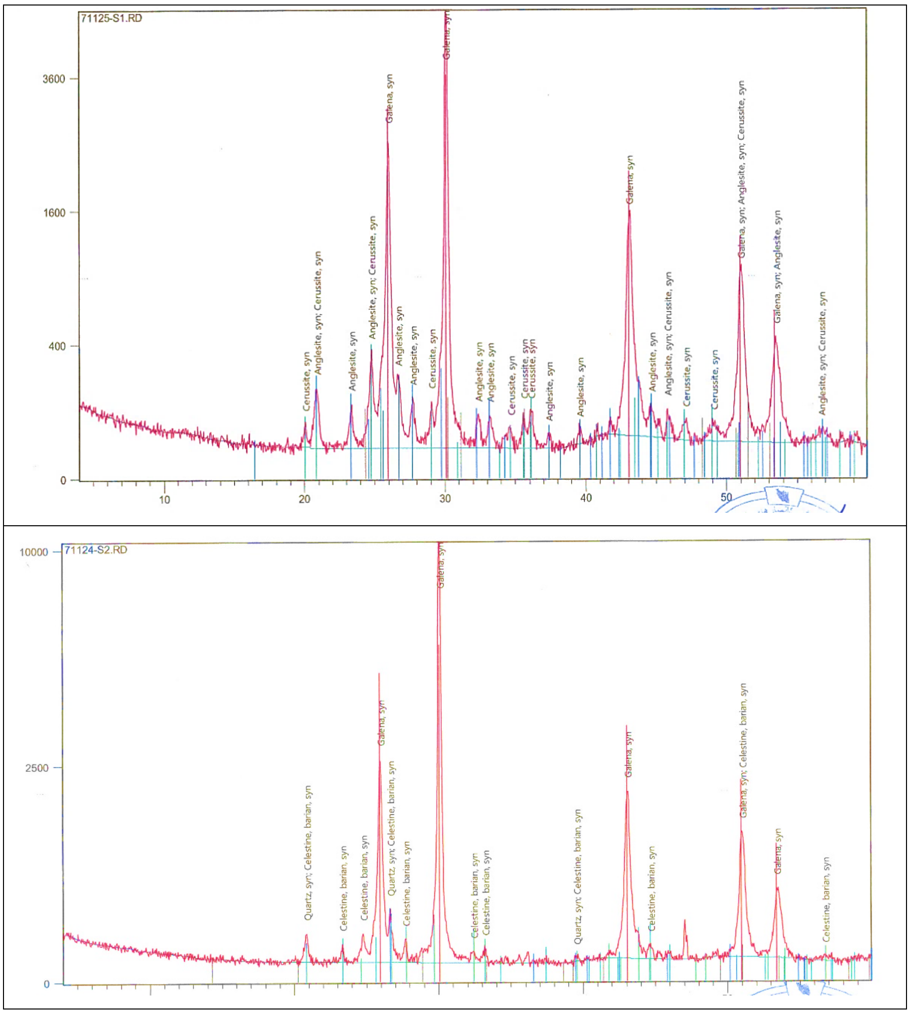

Figure 2. X-ray diffractometer analysis of S_T (left) and S_K (right) to determine the mineralogical composition.

X-ray tube under high vacuum conditions. X-ray diffractometer (XRD) analysis was used to determine the mineralogical composition, both qualitative and quantitative analysis of multiphase mixtures through comparing with minerals database. Two samples, S_T and S_K, were subjected to XRD studies employing Philips X- ray diffractometer (Model PW 1840). Scanning parameters for analyses were Range: 4° -70° 2Θ, Rate: 0.02° 2Θ/sec, Voltage: 40 kV and 30 mA, Radiation: Cu-Kα: 1.54 Angstrom, Scan: fast/continuous.

2.2. Traditional applications of ithmid and recent studies

The indications of *ithmid* in Traditional Iranian Medicine (TIM) were searched in three main manuscripts including *Makhzan al advieh*, *Qarabadin Salehi*, and *Qarabadin Kabir*, applying the keywords of *ithmid*, *kohl*, and *surma* (11-13). Moreover, some studies about anti-microbial activity and mineralogical assays of *ithmid* stone and kohl-based products were pointed out.

3. Results

Major and minor phases of *ithmid* stones, determined by XRD are illustrated in Table 1 and Figure 2. Major component of two samples was galena (PbS). The amount of elements and oxides in three samples of *ithmid* stone determined by XRF are shown in Table 2. SO_3 (9.68 %, 10.60

Table 1. Major and minor phases of two *ithmid* stones, determined by XRD.

Sample	XRD major phase	XRD minor phases
S_T	Galena (PbS)	(Cerussite ($PbCO_3$)) (Anglesite ($PbSO_4$))
S_K	Galena (PbS)	(Quartz (SiO_2))(Celestine (Sr 0.75 SO_4, Ba 0.25)

%, and 11.85 %) and SiO_2 (2.95%, 13.12 %, and 20.50%) had the highest amounts in three *ithmid* samples. The stones also contained MgO, Al_2O_3, Fe_2O_3, CaO, Na_2O, P_2O_5, MnO, K_2O in smaller amounts around 1% or less. The results from XRF proved Pb as the main element of all three samples with high concentrations (625900, 689589, and 766500 ppm). Ba, Sr, Zn, Cl, Cu, Ni, Nb, V, Cd, and Hg were detected in concentrations around 100 to 1000 ppm in *ithmid* samples.

Ithmid had been traditionally presented via ocular, topical, and vaginal routes of administration. Traditional indications for *ithmid* are summarized in Table 3.

Table 2. The amount of elements and oxides in three samples of *ithmid* stone, determined by XRF

oxides (%)	SO_3	SiO_2	MgO	Al_2O_3	Fe_2O_3	CaO	Na_2O	TiO_2	P_2O_5	MnO	K_2O
S_T	11.85	2.95	0.39	0.31	0.28	0.11	0.07	0.03	0.03	0.01	0.01
S_K	9.68	20.50	1.89	1.01	1.16	0.02	2.30	0.13	0.09	0.04	0.02
S_{SH}	10.60	13.12	1.55	1.97	1.69	0.14	0.28	0.28	0.42	0.00	0.14
elements (ppm)	Pb	Ba	Sr	Zn	Cl	Cu	Ni	Nb	V	Cd	Hg
S_T	766500	1286	872	398	316	267	187	31	28	10.6	7
S_K	625900	1458	1035	638	332	281	213	-	33	6.8	5.8
S_{SH}	689589	4073	827	379	272	107	132	6	-	NC*	NC

* NC: not studied

4. Discussion

This study demonstrated that the major phase of *ithmid* samples was galena (PbS), and the main element was Pb with a very high concentration (625900, 689589, and 766500 ppm).

Main indications of *ithmid* based on TIM manuscripts were ocular injuries, infectious wounds, and visual disorders. There are numerous reports that *ithmid* was applied against eye infections by ancient cultures. In recent studies (table 4), kohl-based products have shown antimicrobial effects against pathogens involved in ocular infections (19). The mechanisms involved are reported to be protein dysfunction, production of reactive oxygen species (ROS), depletion of antioxidants, impairment of membrane function, and interference with nutrient assimilation (20).

Lead sulfide nanopowder has shown antibacterial activity against gram-negative bacteria (*E. coli*), gram-positive (*B. cereus*, *S. aureus*), and fungi (*A.terreus*, *A. niger*). The mechanism of action is release of constituent ions and generation of reactive oxygen species (ROS) (21).

Wound healing activity of *ithmid* is associated with its broad antimicrobial property.

Kohl-based products are used as a cosmetic in the Far and Middle East. They are sold in the form of stone, powder, finger rods, or pencils. The general belief is that the black, shiny powder of *ithmid* reflects more light rays leading to less visual damage. Solar protective activity of galena (PbS), the major ingredient of *ithmid*, has been ap-

Table 3. Traditional indications and dosage forms of *ithmid* (11-13).

Dosage form	Indication
ocular	vision loss in elderly
	injuries and infections
	types of headache
	madarosis of eye
	tonic for optic nerves
topical	anal wounds
	burn wounds
	genital wounds
	infectious wounds
	pediculosis
vaginal	hypermenorrhea

Table 4. A summary of the studies about antimicrobial activity and mineralogical assays of kohl-based formulations or *ithmid* stone.

Sample [Number]-source	Microorganism strain(s)	Study output	Sample composition [Analysis method]	Ref
kajal formulations [7] from India	*S. aureus* *P. aeruginosa* *E. coli*	antimicrobial activity of all formulations	-	(14)
traditional kohl-based products [20] from Karachi	*K. pneumonia* *P. aeruginosa* *P. mirabilis* *S. aureus* *S. epidermidis* *C. albicans* *C. tropicalis* *A. flavus,* *F. oxysporum*	good antibacterial activity (3/4 of samples) the highest activity against *P. mirabilis* and *S. epidermidis* antagonistic potential against fungal pathogens (1/3 of samples) the highest activity against *Candida* and *Mucor* sp.	As (in 90% of samples) Cd (in 65% of samples) Pb (in 40% of samples) [Flame Atomic Absorption Spectrophotometery]	(15)
kohl-based products [5] from Saudi Arabia	*S. pyogenes* *P. vulgaris* *S. aureus*	strong antibacterial effect on three microorganisms by lead-containing (88%) product	Pb (0 - 88%) Sb (0 - 9.97%) [Electrothermal atomic absorption spectrophotometry]	(16)
kohl stone [1] & Surma [1] from Madina	-	-	Pb (85%) S (11) Sb (2%) C (0.6%) [XRD-XRF]	(17)
Kohl-based products [12] from Spain and Germany	-	-	Pb (2 - 411000 ppm) Sb (0 - 48 ppm) As (0 - 12.5 ppm) Sb (0 -75 ppm) [Coupled Plasma Optical Emission Spectrophotometer]	(18)

proved. Galena has high absorption and low transmission in the UV light band, so it can be used against harmful effects of sun light to protect the eyes (22). Blood analyses of children, women and men who use kohl products regularly revealed a high lead concentration and low hemoglobin levels (9, 10). Long application of *ithmid* for infants and children can result in lead toxicity. Prenatal exposure due to the maternal exposure with lead sources is linked to neurodevelopmental delays after birth. Therefore, high concentration of lead in maternal blood indicates possible risks for fetus (23). Regular inspection of kohl-based products should be conducted by authorities to detect hazardous products. Continuous application of *ithmid*, the main source of lead exposure, is considered as a potential threat to consumers, specifically for pregnant women and younger children. So, routine quality controls are recommended in order to enforce acceptable limits of potential contaminants in kohl-based products.

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Conflict of Interest

The authors declare no conflict of interest.

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