Letter to the Editor

Elemental analysis, physicochemical characterization and lithotriptic properties of *Lapis judaicus*

Jews stone is the larger spines of regular echinoids, especially cidarooids such as *Balanocidaris glandifera*, called *Lapis judaicus* (English: Jews’ stones; Persian: Sang-e-Jahudan; Arabic: Hajarahul Yahud). It is commonly ornamented by a series of longitudinal, finely tuberculated striae. It was formed in the Late Jurassic (Oxfordian to Tithonian) in Europe, North Africa and the Middle East. The spines have a short neck and a globular head ornamented with beaded ribs. The head tapers rapidly to a point distally. In terms of provenance, spines of *B. glandifera* are most likely to have come from the Upper Oxfordian ‘Glandarienkalk’ limestones of the Mount Hennon district of what is now southern.1

*Lapis judaicus* has a long history of use in both eastern and western traditional medicines for urinary diseases. Moreover, its beneficial properties in the treatment of bowel bleeding, wounds, stings, and snakebites were also noted.2 Dioscorides Pedanius (first century AD) recommended the use of *Lapis judaicus* for dissolving urinary calculi. It should be bruised to make a pulverized powder, suspended in water, and drunk.3 Later medieval European physicians were also recommended this drug for similar indications.4 Ibn Sina, the mediaeval Persian scientist believed that it was one of the most useful drugs for urinary calculi healing.5 A review on historical text of medieval Al-Sham indicated that it was extensively used for internal and skin diseases.6 Specimens of Jews’ stones are still sold in certain bazaars of Iran, Iraq, Afghanistan,7 Jordan,8 India, and Pakistan.9

Beside extensive use of *Lapis judaicus*, information about its chemical constituents and pharmacological activity is very limited. An *in vivo* study showed that it has an inhibitory effect on the crystallization of calcium oxalate.10 We have recently done a double blind randomized clinical trial for evaluation lithotriptic effect of *Lapis judaicus* on patients which have calcium oxalate stone(s) in lower pole of their kidney (clinicaltrials.gov/ct2/show/NCT01443702). In this regards, we will introduce chemical constituents and some physiochemical parameters of this drug. Moreover we will demonstrate *Lapis judaicu* potentials in size reduction of calcium oxalate stones in *vitro*.

*Lapis judaicus* was purchased from different cities in Iran. Fossils were identified by Department of Paleontology, Shiraz University and voucher specimens deposited in Shiraz School of Pharmacy collection.

Various stone shapes were present in the bulk of Jews’ stone. We categorized them depending on their size and morphologic shape. Randomized sampling was done for calculating the percentage of each form. Organoleptic features of the powder were evaluated by observing color, odor, and taste.11 Water, ethanol and acid soluble extracts, pH, total and acid insoluble ash and loss on drying were measured according to methods described in United States pharmacopeia.11 Each study was repeated 6 times.

Samples were analyzed for their carbon, hydrogen and nitrogen (CHN) concentration on a Costech ECS 4010 Elemental combustion system (Valencia, CA) with pneumatic auto sampler. It was set up for CHN analysis. Reactor 1 consisted of chromium (III) oxide/silvered cobaltic–cobaltic oxide catalysts at 980 °C. Reactor 2 consisted of reduced high purity copper wires at 650 °C. Helium was used as the carrier gas at a flow rate of 100 mL min⁻¹. This was filtered for hydrocarbons upstream of the instrument. A packed (Porous polymer, HayeSep Q) 3 m GC column (SS 6 × 5 mm –2m–HayeSep q 60/80) was used for separation of the gases. A thermal conductivity detector (TCD–L–3) was used to calculate the signal of each sample. Three 10% *Lapis judaicus*/n-hexane powder (w/w) extracts were prepared by maceration method for 24 h. The resulted extracts were filtered and kept in –20 °C for injection to Gas chromatography–mass spectrometry (GC/MS). The GC/MS analyzes were carried out using a Hewlett-Packard 6890. The gas chromatograph was equipped with an HP-5M capillary column (phenyl methyl siloxan, 25 m × 0.25 mm i.d., Hewlett-Packard Part No. 190915.433, USA). The oven temperature was programmed from 50 °C (3 min) to 250 °C at the rate of 3 °C/min and finally held for 10 min at 250 °C. The carrier gas was He with the flow rate of 1.2 mL/min. The mass spectrometer (Hewlett-Packard 5973, USA) was operating in EI mode at 70 eV. The interface temperature was 250 °C; mass range was 30–600 m/z. Identification of components was based on a comparison of their RI and mass spectra with Wiley (275).12

A wavelength-dispersive sequential X-ray spectrometer (PW 25040, Philips, The Netherlands) equipped with super-Q software for quantitative analysis was used for measuring the Kα line of all elements.

Crystal identifications were carried out on a X-ray powder diffraction (XRD) analyzer (Xpert–MPD, Philips, The Netherlands) system operating at the Co Kα wavelength of 1.7889 Å, 30 mA, and 40 kV. Step size was 0.02°/s.

The samples were detected for presence of heavy metals such as lead, arsenic and mercury. Determination of heavy metals was done.
We added 1 g of Lapis judaicus powder to a 250 ml beaker, which contain 100 ml of phosphate buffer (pH = 6.0). For negative control, nothing was added to the buffer. Calcium oxalate calculi expelled by surgery from patients weighed and put in each the buffer. For each group (Lapis judaicus and control) we used four samples. Beaker shacked and after 48 and 120 h the weight changes were measured. As there is not any standard drug for size reduction in calcium oxalate stone, we didn’t have positive control.

Jews’ stones have a variety of morphological presentations (Fig. 1). Genser (1565) and Mercati (1791) were also reported these variations. Olive shape (77.13% w/total weight) and bone shape (15.21% w/total weight) are major morphologies (Table 1). Olive, bone and spindle shapes are Echinoid fossils and shell shapes are Goniorhynchia fossils. The powder is Khaki in color and without noticeable taste or odor. Loss of weight on drying was found to be 3.13 ± 0.97 w/w, which is not too high, hence could limit bacterial, fungal, or yeast growth. Extractive value was low in water (4.33 ± 0.32 w/w) and ethanol (5.00 ± 0.01 w/w). However, its solubility in acid was high (94.87 ± 0.99 w/w) which may indicate high solubility in gastric syrup. The pH of 1% and 10% w/w solution was nearly 9.52 ± 0.01 and 9.25 ± 0.04 respectively, which indicates basic behavior of Jew’s stone in solution. Total ash value was 38.35 ± 9.47 w/w which 22.24 ± 5.13 w/w was soluble in acid.

CHN elemental analysis indicated that Lapis judaicus powder conation 26.55 ± 1.24% carbon, 0.97 ± 1.24% hydrogen and almost no nitrogen. In average, carbon, hydrogen and nitrogen are 27.68 ± 1.43% w/w of total powder. In the other hand, GC/MS apparatus did not find any significant compound in the prepared extracts. Based on CHN and GC/MS results we didn’t find any organic material in Lapis judaicus.

X-ray fluorescence semi quantitative results that almost 43.76% of materials were lost on ignition. Major components of the powder after ignition were CaO (52.44 W/W), MgO (1.75% W/W), SiO₂ (1.07% W/W), Fe₂O₃ (0.50% W/W), Al₂O₃ (0.33% W/W) and Sr (0.08% W/W). Moreover, trace amounts (less than 0.001%) of Phosphorus, Chlorine, Nickel, Palladium, Sodium, Sulfur, Titanium, Chromium, Copper, Potassium, Manganese, Gallium, Bismuth, Ruthenium, Indium and Cerium were founded. Elemental analysis of different morphologies presented in Lapis judaicus showed that chemical constitutes in different morphologies were almost similar although the percentage of some constitutes are different (Table 1). X-ray powder diffraction qualitative identifications lead to identifying five different mineral crystals in Lapis judaicus powder. These minerals were Calcite (CaCO₃), Dolomite (CaMg(CO₃)₂), Quartz (SiO₂), Boehmite (Al₂O₃(H₂O)) and Muscovite (KAl₂(AlSi₃O₁₀)(OH)₂). Moreover, no heavy metals were identified by atomic absorption spectrometer method (<1 ppb).

In vitro studies indicated that Lapis judaicus powder can reduce the size of calcium oxalate stones 35.1 ± 7.9% after 2 days and 58.2 ± 1.64% in 5 days (p < 0.05).

Inorganic materials have been in the inventory of medicinal substances of various cultures since ancient times. Most of them and their usage did not fade away when modern medicine took over; they exist to the present day in the traditional systems of medicine around the world. Traditional healers have used them alone or combined with a wide array of other geological and botanical ingredients, to treat a diversity of ailments. Unlike medicinal plants for which WHO has issued of official standardization methods, there is no official standardization reference for inorganic substances used in traditional medicines.

This study, not only investigated physicochemical properties of Lapis judaicus, but also chemical constitutes and in vitro pharmacological activities. Lapis judaicus contain magnesium, which is a protective agent in calcium oxalate crystal growth. Moreover its basic pH nature could be another inhibitor for stone production. Furthermore SiO₂ can change calcium oxalate monohydrate to calcium oxalate dihydrate, which is more soluble. In the other hand...
A high amount of calcium makes a controversy because it is a promoter for calcium oxalate crystallization. Results of an in vitro study indicated that *Lapis judaicus* could be a candidate for future studies in the field of renal stone dissolving agents.

The results obtained in this study is not only useful for researchers in the filed of urinary stones but also considered as a showcase for determining authenticity and purity of non-organic traditional drugs for quantitative standardization.

**References**


Pouya Faridi
Department of Traditional Iranian Pharmacy, Pharmaceutical Sciences Research Center, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz 71345 1583, Iran
E-mail address: faridip@sums.ac.ir (P. Faridi)

Hassan Seradj
Department of Pharmacognosy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz 71345 1583, Iran
E-mail address: serajh@sums.ac.ir (H. Seradj)

Soliman Mohammadi-Samani, Prof.
Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz 71345 1583, Iran
E-mail address: smsamani@sums.ac.ir (S. Mohammadi-Samani)

Jamshid Roozbeh, Prof.
Department of Internal Medicine, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz 71345 1583, Iran
E-mail address: roozbehj@sums.ac.ir (J. Roozbeh)

Abdolali Mohagheghzadeh, Prof. *Corresponding author. Tel.: +98 711 2425374; fax: +98 711 2426070. E-mail address: mohaghegh@sums.ac.ir (A. Mohagheghzadeh)*

*Available online 14 March 2013*