



Biological and Geochemical Studies of Urinary Tract Stones in Lorestan Province

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ABSTRACT

Mineralogy studies can help understand the interactions of geographical, environmental, and geological factors. Considering frequent occurrence of urinary tract stones in the south and west of Iran, the present paper examines trace elements, like heavy metals, in 53 urine stone samples collected from patients in Lorestan Province. It investigates the mineralogy of the stones, using X-ray diffraction. The samples are then classified into five mineral groups (calcium oxalate, urate, cysteine, calcium oxalate-urate, and calcium oxalate/phosphate). Results from this analysis are confirmed by SEM images, showing the crystalline form of the mineral phases. The microscopic studies show that only the mineral group of calcium oxalate (whewellite) could be detected in thin sections, prepared from urinary tract stone samples. The main and trace elements in each group are determined through ICP-MS method with the results showing that calcium is the most abundant substance in urinary tract stones, compared to other elements. This is caused by the role of calcium in most basic functions of cell metabolism. The correlation between magnesium and strontium is 0.64, originated from the placement of high amounts of strontium in calcium oxalate minerals. The positive correlation between sodium and calcium also indicates that sodium is replaced by calcium due to the similarity of the ionic radius in the crystal structure. Results from this study can help us find the causes behind the frequent occurrence of urinary tract stones in Lorestan Province.

Keywords: Mineralogy, Scanning electron microscope, Calcium oxalate, Urinary tract stones

INTRODUCTION

The relationship between human health and the environment involves many complex interactions (Rani et al., 2020). Environmental hazards can have a wide range of health effects. Most important diseases are associated with more than one type of environmental risk, which themselves interact with genetic factors, nutrition, lifestyle risks, and other pathogens (Cepon et al., 2021). Stone formation in urinary tracts of human bodies is the most common and painful urinary disorder around the globe (Aragon et al., 2018). Urinary tract stones are considered biological minerals that can be classified into several groups, based on their mineralogical composition, among which, calcium oxalate, calcium phosphate, uric acid, and struvite stones are the most common types (Chandrajith et al., 2019). Although kidney stones have been studied for decades, their etiology is still not understood well. The urinary tract stone disease is influenced by factors such as environmental conditions, dehydration, geochemical factors (Abeywickrama et al., 2015), internal disorders in individuals, mineral metabolism, and biological factors, as well as the impact of other diseases like cardiovascular disease and diabetes, or a combination of both (Zarasvandi et al., 2014; Durgawale et al., 2010). The average prevalence of urinary tract stones during a lifetime may be up to 20% in

the general population (Lohia et al., 2017). The percentage of patients with urinary tract stones in different parts of the world varies between 20% and 30% (Safarinejad., 2007). Moreover, men suffer from urinary tract stones more than women (Wang et al., 2019). In recent decades, the prevalence of this disease has been closely related to changes in lifestyle, industrialization, and changes in dietary patterns. These recent changes in environmental factors have been associated with a lack of fiber in the diet, excessive consumption of animal proteins, calcium, and salt, hot and dry climates, alcohol consumption, lack of physical activity and exercise, and a low-potassium diet. Among environmental factors, hardness of water is the most important factor to cause kidney stones (Esmail et al., 2020). The ratio of magnesium to calcium has also been shown to correlate with urinary tract stones (Wang et al., 2021).

Iran is one of the critical regions located in the Africa-Asia stone belt with different climatic conditions. The prevalence of kidney stones varies with an average rate of 5.7% in different parts of Iran. Kidney stones occur more in the south and west of the country; that is why, it is very important to determine the type of stone and study recognize the factors leading to this disease (Yavarshayeri et al., 2014). Analysis and mineralogical studies of urinary tract stones and the crystallization process are of particular importance in determining the possible environmental and pathophysiological reasons for stone formation. This study aims at investigating the mineralogy and stable isotope compositions in urinary tract stones in Lorestan Province in southwestern Iran.

MATERIAL AND METHODS

With an area of 28306 km², Lorestan Province is located in the western part of Iran between 46° 50' to 50° 1' E and 32° 40' to 34° 23' N, in the Greenwich meridian (Japlaghi Et al., 2017). The minimum altitude of the province belongs to Pol Zal, being 330 m, and the maximum altitude to Oshtrankooch, equal to 4050 m (Delfan et al., 2014). The province has nine cities and its capital is Khorramabad. Geographical factors such as climate, altitude and unevenness, water resources, soil quality, vegetation, and relative position play a key role in dispersing the population in Lorestan Province (Japolghi et al., 2017). Fig.1 illustrates the geographical location of the study area.

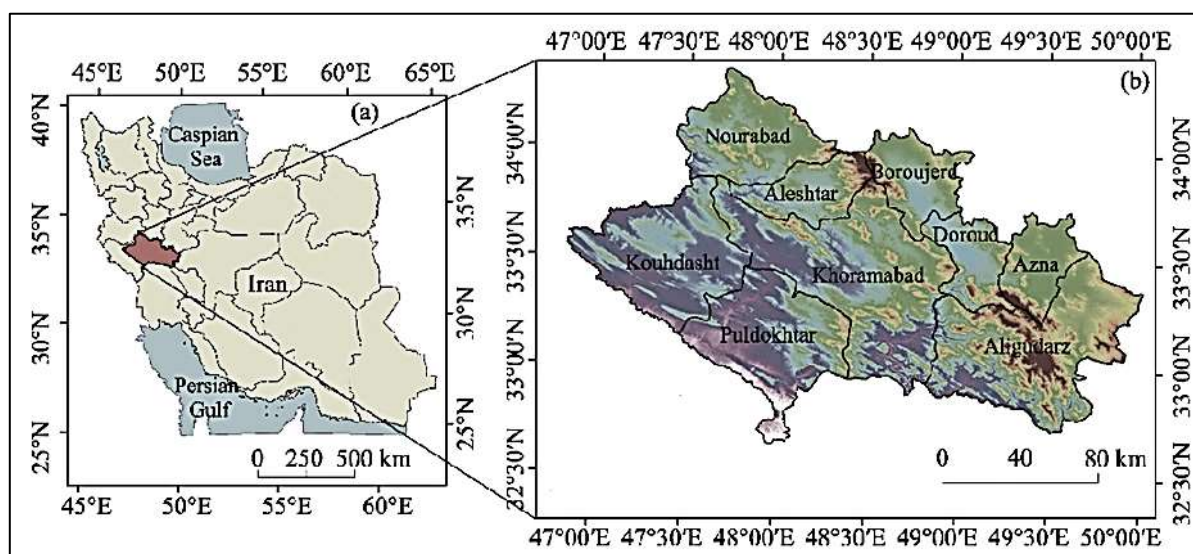


Fig.1. The geographical location of Lorestan province

In this study, fifty-three urine samples were collected from hospitals in different cities of Lorestan Province in southwestern Iran (Fig.2). After collecting the samples, patients' personal information such as age, sex, weight, medical history, and address before surgery were recorded in a questionnaire. Each sample was washed several times with distilled water to remove urine, blood, and organic matter residues. Once dried, the samples were kept in a polyethylene container in the laboratory before getting crushed.



Fig.2. The studied urinary tract stones

To study the correlation of mineralogical and optical properties of kidney stones with the obtained chemical composition, ten samples got selected to prepare thin sections. They were studied with a polarizing light microscope in the mineralogy laboratory. Also, ten stone samples were sent to Razi Metallurgical Studies Center of Tehran to obtain the crystalline phase for X-ray diffraction (XRD) analysis. Scanning Electron Microscopy (SEM) was used to study the size, system, shape, and name of the constituent minerals as well as the elemental composition of different parts of urinary tract stones. For this purpose, ten samples of urinary tract stones were analyzed at Razi Research Center of Tehran with field emission scanning electron microscopy model, MIRA3 TSCAN-XMU.

To determine the concentration of major and minor elements in the selected samples, ten samples of kidney stones were measured in the geochemical laboratory, using the ICP-MS method. In this analysis, as much as 0.25 g of each sample was heated with HF, HCl₄, and HNO₃ acids at 200 ° C for 4 to 5 h. Then, for complete digestion, the samples were dissolved in HCl acid and the elements' concentration was read.

Based on the study of Beyrami et al. (2016), in the X-ray diffraction (XRD) method, the Limit of Detection (LOD) and Relative Standard Deviation (RSD) were 0.45-0.3 and 2.8-0.4 mg/ l, respectively. Therefore, the maximum error of this method's results was $\pm 5\%$.

RESULTS AND DISCUSSIONS

One of the limitations of this study was the small number of analyzed samples ($n = 53$). Hence, all the conclusions made in this section are experimental. Among the patients, 60% were male and 40% were female. Table 1 gives the distribution of urinary tract stones according to the age and sex of patients.

Since one of the important factors for the formation of urinary tract stones pertains to the characteristics of drinking water in each region, the main components in the occurrence of water hardness in Lorestan Province were measured, whose results are presented in Table 2.

The prevalence of urinary tract stones was higher in patients, aged between 40 and 60 years. A significant increase in calcium oxalate (25%) and mixed stones (22.5%) in the ages of 40 to 60 years shows an increase in the prevalence of the mineral group with age.

Calcium oxalate and uric acid stones are more prevalent in men than women. Daudon et al. (1993) also showed that calcium oxalate and urate stones are more common in men than women. Phosphate and cysteine stones make up a small percentage of urinary tract stones.

Table 1. The classification of urinary tract stones based on age and sex ratio in the study area (Source: Present Research)

Age group	Calcium oxalate		Uric Acid		Cysteine		Phosphate		Mixed stones	
	men	women	men	women	men	women	men	women	men	women
40<	-	2	2	-	1	2	-	1	1	1
40-50	3	-	2	-	-	1	-	-	3	1
50-60	3	4	-	1	-	-	1	-	4	1
60>	2	-	-	1	-	-	-	-	2	1

Examination of the morphological structure of the selected stones by means of a polarizing light microscope showed that only the mineral group of calcium oxalate (Whewellite) could be detected in thin sections, prepared from urinary tract stone samples. In addition to whewellite mineral, the biominerals calcium, silica carbonate, amorphous, and iron oxide were also present in some samples.

Table 2. Average results obtained from components related to the water hardness in different cities of Lorestan Province

PO ₄	SO ₄	Cl	Na	K	Mg	Ca	TDS (ds/m)	EC (μ mho/cm)	City
0.15	249.00	44.00	30.50	1.60	13.10	86.60	285	475.00	Khorramabad
0.29	252.00	8.50	5.00	0.22	5.30	65.90	345	575.00	Borujerd
0.26	168.00	41.50	24.00	1.40	23.00	53.00	391.2	652.00	Kouhdasht
0.32	189.50	44.50	66.30	1.78	19.34	87.54	343.8	573.00	Noorabad
0.49	160.34	31.73	15.32	1.93	23.09	45.33	259.2	432.00	Aligudarz
1.62	463.00	68.20	109.10	2.55	13.88	117.38	494.4	824.00	Poldokhtar
0.87	253.00	18.32	9.43	0.98	26.84	59.38	160.2	267.00	Aleshtar
0.23	192.00	8.38	9.54	0.52	6.45	87.40	258	430.00	Dorud
0.83	153.00	99.50	25.80	1.10	9.87	101.30	233.4	389.00	Azna

The radial layer texture with the periodicity of brown and light brown to colorless minerals is one of the characteristics of calcium oxalate minerals, especially whewellite (Afaj et al., 2005). An amorphous nucleus in the center of concentric layers is another feature of the calcium oxalate group (Abboud., 2008b). Fig. 3a and 3b show a whewellite mineral with a radial texture growing inwards from the margin with a high amount of iron oxide. The presence of iron in calcium oxalate stones may be caused by trapping the iron ions on the

crystal surface or in the crystal lattice (Bazin et al., 2007).

There are many different types of biomaterials, one of the most common compounds of which is calcium carbonate with calcite polymorphs (McGrath, 2001). Fig. 3c represents calcite biominerals with self-forming texture. The presence of these biomaterials indicates that in addition to whewellite minerals, biominerals are also effective in the formation of urinary tract stones.

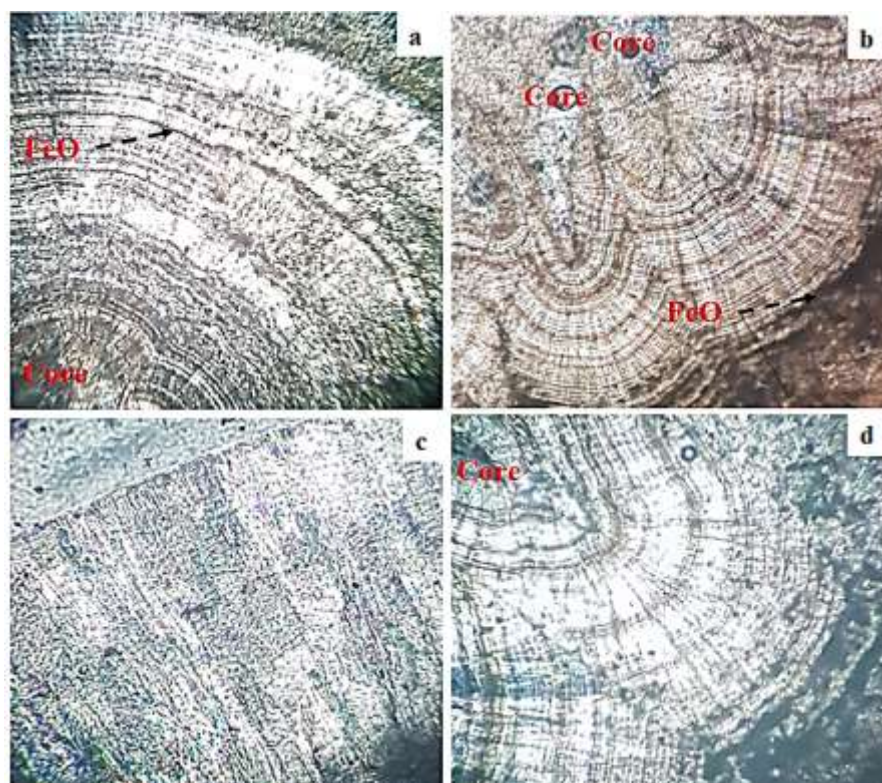


Fig.3. a) The concentric and radial layer (a, b, and d), the characteristic of calcium oxalate stones; b) The whewellite mineral in brownish yellow color; c) The presence of calcite crystals in urinary tract stones

Table 3 represents the mineralogical results of urinary tract stones, collected from different regions of Lorestan Province, using X-Ray Diffraction (XRD) Method. X-ray diffraction data show the presence of whewellite mineral ($C_2CaO_4 \cdot H_2O$), oricite ($C_4(NH)_2O_2C(NH)_2O$), cysteine ($C_6H_{12}N_2O_4S_2$), and hydroxyapatite ($Ca_5(PO_4)_3(OH)$) in studied urinary tract stones. According to Table 3, the urinary tract stones are in 5 groups of calcium oxalate, urate, cysteine, calcium oxalate-urate, and calcium oxalate/phosphate.

Table 3. The mineralogy of urinary tract stones collected from Lorestan Province, using XRD method

The percentage of abundance	number of samples	Sub-minerals	main minerals	Mineral group
35	14	-	Whewellit.	calcium oxalat
15	6	-	Oricite	Uric Acid
10	4	-	Cysteine	Cysteine
5	2	hydroxyapatite	Whewellit	Calcium phosphate
20	8	Uric Acid	Whewellit	Mixed stones
15	6	hydroxyapatite	Whewellit	

The most common group (35%) is calcium oxalate stones and the second largest, calcium oxalate/uric acid mixed stones (20%). Also, 15% belongs to the uric acid group. Calcium oxalate/phosphate stones (15%) and cysteine (10%) form urinary tract stones (Fig.3) and are in the next places.

Scanning electron microscopy (SEM) images also confirm the results of X-ray diffraction analysis. Calcium oxalate minerals such as Whewellite, which can be detected by the monoclinic system and plate morphology (Abboud, 2008), can be clearly seen in SEM images of urinary tract stones (Figs.3a and b). SEM image (Fig.3c) shows uric acid crystals with the structure of monoclinic, polymorphic, and prismatic (Giannossi and Summa, 2012). Sometimes due to the changes in urine pH, crystals of uric acid and calcium oxalate are found together in the stone.

The presence of oricite with whewellite indicates a change in the pH of the urinary system (Lay et al., 2019). In the urinary system with $\text{pH} < 6$, uric acid crystals precipitate, leading to the formation of uric acid stones. However, when the urinary system becomes alkaline, uric acid remains in the solution and does not precipitate. Therefore, the conditions are favorable for the formation of calcium oxalate crystals like whewellite.

These changes may be caused by environmental factors such as nutrition, the drinking water, and metabolism (Hesse et al., 2009). Fig. 3d shows that the calcium oxalate (Whewellite) crystals are arranged as a plate on a rocky background. Moreover, large and prismatic urate crystals are found among calcium oxalate minerals. In addition to the calcium oxalate and urate minerals, phosphate minerals such as struvite are also seen in the SEM images with the whewellite mineral, formed under alkaline conditions, being similar to calcium oxalate minerals.

Determining the concentrations of alkaline, alkaline earth, and phosphate minerals as well as similar compounds are of great importance in environmental studies. Furthermore, there is a higher concentration of some elements like Na, Cu, Mg, S, Ca, P, and Mn in the urinary tract stones, formed in different parts of the urinary system. The presence or absence of some elements in the body is one of the factors affecting the formation of urinary tract stones (Touryan et al., 2004).

Table 4 shows the results of induced coupled plasma mass spectrometry (ICP-MS) of urinary tract stones in 10 samples. Calcium is the most abundant element in stones, compared to other elements due to its role in most basic functions in cell metabolism. Calcium is a major component of urinary tract stones.

Calcium affects urinary tract stones, depending on water and the type of food, such as milk, dairy products, egg, tea, and hard water (Robertson et al., 1980). Sodium, phosphorus, and sulfur are also abundant in urinary tract stones. Relatively high amounts of magnesium, iron, and potassium are present in all analyzed samples. Table 4 gives the results of induced coupled plasma mass spectrometry (ICP-MS) of urinary tract stones of Lorestan Province in terms of (PPM).

Bivalent ions (such as zinc and strontium) are more likely to be substituted in calcium-containing stones (Bazin et al., 2007). In these stones, the amount of heavy metals (such as zinc and strontium) in Vodolite is higher than whewellite (Joost and Tessadri, 1987). Similarly in the present paper, the concentrations of zinc and strontium in the calcium oxalate group with the mineral phases of Vodolite and Whewellite (208 ppm and 230 ppm, respectively) were higher than the mineral phase of pure Whewellite (69 ppm and 73 ppm).

Table 4. The results of induced coupled plasma mass spectrometry (ICP-MS) test of urinary tract stones in Lorestan Province in terms of PPM

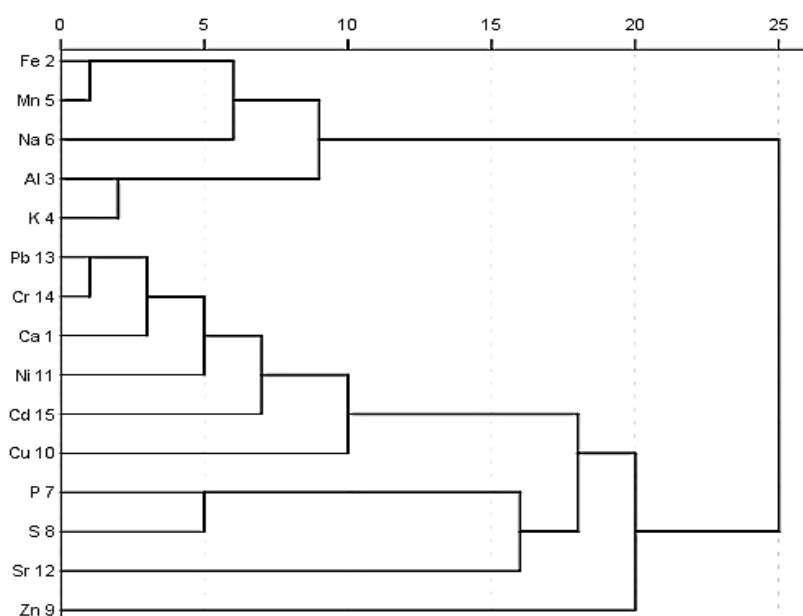
Element	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Sample7	Sample8	Sample9	Sample10
Calcium(%)	8.1	6.4	9.6	9.2	8.4	8.8	9.7	9.8	8	10
iron(ppm)	463	156	473	410	502	499	523	399	312	405
aluminium(ppm)	316	128	229	276	324	628	212	254	220	293
potassium(ppm)	536	215	580	478	756	1305	720	553	615	407
magnesium(ppm)	315	128	394	302	500	557	543	386	309	306
Sodium(ppm)	1053	890	1327	1802	2155	2550	1865	1954	2281	1830
phosphorus(ppm)	1598	5491	8915	7540	2763	3951	3529	4915	2945	3663
sulfur(ppm)	2117	3424	5442	5311	909	2374	3561	2206	3571	2256
zinc(ppm)	29	57	48	117	48	76	62	43	44	52
copper(ppm)	6.1	12.3	11	14.6	13.5	8.6	8.4	9.9	17.4	10.2
nickel(ppm)	0.9	1.5	1.3	1.4	0.9	1.4	1.2	1.5	1.2	0.7
Strontium(ppm)	54	4.1	209	96	104	73	86	103	187	74
lead(ppm)	6.6	8.3	8.9	6.9	5.1	6.8	64.2	7.8	7.1	1.8
chrome(ppm)	8.3	11.4	7.6	6.7	8.9	7.2	7.1	8.6	8	9.2
cadmium(ppm)	0.26	0.4	0.25	0.23	0.28	0.21	0.27	0.22	0.26	0.22

The concentration of elements in urinary tract stones depend on the mineral phase (Golovanova et al., 2006). The concentration of zinc in Vodolite is higher than whewellite, since Vodolite is formed during the crystallization process, then to convert into whewellite where zinc is likely to be released (Giannossi et al., 2012).

Thus, trace elements can help stabilize calcium oxalate dihydrate (Vodolite) (Hesse et al., 1988). Concentrations of zinc and strontium in mixed stones indicate different phases within the stone (Perk et al., 2002). The amount of iron in non-calcium stones (uric acid and cysteine) is less than calcium stones (calcium oxalate). High levels of iron may be due to the inhibitory property of Fe^{+3} during the crystallization of calcium oxalate (Meyer and Thomas, 1982; Munoz et al., 2005). Meyer and Angino (1997) showed the inhibitory effect of copper on calcium phosphate stones. However, they recorded no effect on the crystalline growth of calcium oxalate. The correlation coefficient between different elements and their cluster analysis dendrogram is presented in Table 4 and Fig.4, respectively. The positive correlation between sodium and calcium ($r = 0.47$) indicates that sodium is replaced by calcium due to the similarity of the ionic radius in the crystal structure (Abboud, 2008). The positive correlation between magnesium and phosphorus ($r = 0.8$) indicates magnesium's tendency to enter the structure of phosphate minerals. Magnesium is an important element in biological classification (Atakan et al., 2007), being originated from the increase in the magnesium concentration in the human body (Deeming and Webu, 1977). The exact role of magnesium in kidney stone formation has not yet been fully elucidated (Kohri et al., 1988; Siner et al., 2004). Food and hard water along with some drugs are responsible for the amounts of magnesium (Giannossi et al., 2013). It is one of the main components of phosphate stones, where it is precipitated with ammonium and phosphate in alkaline urine (Keshavarzi et al., 2015). A negative correlation between calcium and potassium ($r = -0.04$) indicates that these two elements have different geochemical properties. The reason for the positive correlation between sodium and phosphorus can be attributed to the strong affinity of alkali metals and phosphorus in urinary tract stones (Keshavarzi et al., 2015).

Table 5. The Pearson correlation coefficient between the elements

	Ca	Na	P	S	Mg	Fe	K	Sr
Ca	1							
Na	0.47	1						
P	0.34	0.72	1					
S	0.29	0.39	-0.1	1				
Mg	0.53	0.92	0.8	0.29	1			
Fe	0.25	0.31	-0.17	0.28	0.36	1		
K	-0.4	0.41	-0.77	0.24	0.33	0.7	1	
Sr	0.58	0.46	0.52	0.93	0.64	0.34	-0.19	1

**Fig.4.** The dendrogram of elements' cluster analysis in the 10 samples

The positive correlation of phosphorus and calcium with strontium may be associated with the replacement of this element with calcium and phosphorus in oxalate stones. Calcium and strontium compete for placement in the calcium oxalate structure as a result of their similarities in the metabolic process (Abboud, 2008). Here, the correlation between magnesium and strontium was 0.64, originated from the placement of high amounts of strontium in calcium oxalate minerals. Different distribution of trace elements between calcium and non-calcium urinary tract stones is due to the tendency of some similar ions such as strontium in terms of charge and size with the radius of calcium, entering the crystal structure of calcium urinary tract stones during the replacement processes (Bazin et al., 2007).

Table 6 compares the average concentrations of elements in the present study with studies from other parts of the world. Differences among elements' distribution in urinary tract stones, collected from different regions are likely related to geology, drinking water quality, diet, and treatment facilities. Therefore, it is not surprising that the urinary tract stones collected from Lorestan Province differ from other parts of the world such as Jordan, Sri Lanka, and Italy.

Table 6. Comparison of element concentrations in urinary tract stones of Lorestan Province with other parts of the world

Basilica (Italy) ^b (%)	Jordan ^b	Czech Republic ^a	Khuzestan province ^a	Fars province	Sri Lanka ^a	Present study ^a	element
17.23	20.33	24.8	15.21*	14.76	-	8.8	Calcium
1.63	3.08	400	0.52*	600	9829	374	magnesium
-	0.9	300	0.08*	1300	747.5	616.5	potassium
-	1..56	1200	0.13*	1500	2740.25	1770.7	Sodium
0.9	10.35	500	4.22*	9500	-	4531	phosphorus
-	1.88	-	1.14*	18500	-	3117.1	sulfur
0.26	3.08	48	-	82	35.8	414.2	iron
-	0.49	6	0.04	154	20.94	288	aluminum
0.57	0.19	1.1	39.8	5.1	9.88	11.2	copper
0.05	-	4.4	5.17*	12.1	2.47	7.2	lead
0.45	0.7	67	36.95	83	236.6	57.6	zinc
-	0.31	49	108.5	141	31.37	109	Strontium
0.03	0.15	0.05	-	7.3	0.95	8.3	chrome
-	0.14	0.2	3	9.2	2.21	1.2	nickel
Giannossi et al (2013)	Abboud (2008)a	Kuta et al. (2013)	Zarasvandi et al (2013)	Keshavarzi et al(2015)	Chandrajith et al(2019)	-	reference

* Amounts of major oxides(%)

a Calcium is reported as a percentage and the rest of the elements are in ppm.

b All data are reported as a percentage.

Results from this study show that the main elements such as calcium, magnesium, and potassium at the urinary tract stones of the studied area are less concentrated than other areas. Iron, aluminum, and lead in the samples of Lorestan Province have higher values, compared to other places.

CONCLUSION

Mineral resources play a major role in human life, including food and medicine supply and mineral water storage, to name but a few. However, it is always essential to consider the destructive effects of some minerals on the environment and the well-being of animals that limit the use of mineral resources. Today, the pathogenicity of some minerals and their deadly effects on human health have been proven. Based on the results of mineralogical studies, using the X-ray diffraction method, urinary tract stones of Lorestan Province belong to 5 groups of calcium oxalate, urate, cysteine, phosphate, and mixed stones. SEM images confirm the results of this analysis. The results of induced coupled plasma mass spectrometry (ICP-MS) showed that calcium enjoyed the lion's share, in comparison with other elements in the stones. The results were also compared with some other parts of Iran, e.g., Khuzestan and Fars Provinces as well as other countries like Sri Lanka, Jordan, Czech Republic, and Italy. It was revealed that the main elements such as calcium, magnesium, and potassium in the studied urinary tract stones were less concentrated here than other areas.

A positive correlation between sodium and calcium indicates that sodium is replaced by calcium due to the similarity of the ionic radius in the crystal structure. Also, the positive correlation between magnesium and phosphorus indicates the tendency of magnesium to enter the structure of phosphate minerals.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript. Furthermore, the ethical issues have been completely observed by the authors including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy.

LIFE SCIENCE REPORTING

No life science threat was practiced in this research.

REFERENCES

- Abboud, I. A. (2008). Mineralogy and chemistry of urinary tract stones: Patients from North Jordan. *Envi. Geoch. and Heal.*, 30(5), 445–463.
- Abboud, I. A. (2008a). Analyzing correlation coefficients of the concentrations of trace elements in urinary tract stones. *Jor. J Eart and Env. Scie.*, 1(2), 73–80.
- Abboud, I. A. (2008b). Concentration effect of trace metals in Jordanian patients of urinary calculi. *Jor. J Eart and Env. Scie.*, 30(1), 11–20.
- Abeywickrama, B. Ralapanawa, U. and Chandrajith, R. (2015). Geoenvironmental factors related to high incidence of human urinary calculi (kidney stones) in Central Highlands of Sri Lanka. *Environ Geochem Health*, pp. 1-12
- Afaj, A. H. and Sultan, M. A. (2005). Mineralogical composition of the urinary tract stones from different provinces in Iraq. *The Scientific World Journal*, 5, 24–38.
- Aragon, I. M., Herrera-Imbroda, B., Queipo-Ortuño, M. I., Castillo, E., Del Moral, J. S. G., Gomez-Millan, J. and Lara, M. F. (2018). The urinary tract microbiome in health and disease. *Eur.Uro. Foc.*, 4(1), 128-138.
- Atakan. I. H., Kaplan. M., Seren. G., Aktoz. T., Gül. H. and Inci. O. (2007). Serum, urinary and stone zinc, iron, magnesium and copper levels in idiopathic calcium oxalate stone patients. *Inte. Uro and Nep.*, 39(2), p: 351-356.
- Bazin, D., Chevallier, P., Matzen, G., Jungers, P, and Daudon, M. (2007). Heavy elements in urinary tract stones. *Urolo. Res.*, 35(4), 179–184.
- Beirami. S., Barzoki. H. and Bahramfar, N. (2016). Application of response surface methodology for optimization of trace amount of diazinon preconcentration in natural waters and biological samples by carbon mesoporous CMK-3, *Biomedical Chromatography*. 2017;31: e3874.
- Cepon-Robins, T. J., Blackwell, A. D., Gildner, T. E., Liebert, M. A., Urlacher, S. S., Madimenos, F. C. and Sugiyama, L. S. (2021). Pathogen disgust sensitivity protects against infection in a high pathogen environment. *Proceedings of the National Aca. Sci.*,

- 118(8).
- Chandrajith, R., Weerasingha, A., Premaratne, K. M., Gamage, D., Abeygunasekera, A. M., Joachimski, M. M. and Senaratne, A. (2019). Mineralogical, compositional and isotope characterization of human kidney stones (urolithiasis) in a Sri Lankan population. *Envi. geoch and hea.*, 41(5), 1881-1894.
- Daudon, M., Bader, C. A., Jungers, P., Beaugendre, O. and Hoarau, M. P. (1993). Urinary calculi: review of classification methods and correlations with etiology. *Sca. Mic.*, 7(3), 32.
- Deeming. S. and Weber. C. (1977), Evaluation of hair analysis for determination of zinc status using rats. *Ame. J. Clin Nut.*, 30(12), 2047-2052.
- Delfan, B., Bahmani, M., Eftekhari, Z., Jelodari, M., Saki, K. and Mohammadi, T. (2014). Effective herbs on the wound and skin disorders: an ethnobotanical study in Lorestan province, west of Iran. *Asi. Pac. J. Tro. Dis.*, 4, S938-S942.
- Durgawale, P., Shariff, A., Hendre, A., Patil, S. and Sontakke, A. (2010). Chemical analysis of stones and its significance in urolithiasis. *Biom. Res.*, 21: 305-310.
- Esmail, A. O., Qadir, B. A. and Hamad, H. Q. (2020). Effect of Drinking Water Hardness on Kidney Stones Formation in Ranya District. *Cih. Univ. Erbil. Scie. J*, 4(1), 1-6.
- Giannossi. M. L. and Summa. V. (2013). An Observation on the Composition of Urinary Calculi: Environmental Influence. *In. Medi. Geoch (p: 67-90)*. Medical Geochemistry. Springer, Dordrecht. doi /10.1007/978-94-007-4372-4_5
- Giannossi. M. L., Summa. V. and Mongelli. G. (2012). Trace element investigations in urinary tract stones: A preliminary pilot case in Basilicata (Southern Italy). *Journal of Tra Elem in Medi and Bio.*, 27(2), p: 91-97.
- Golovanova. O., Palchik. N., Maksimova. N. and IN. A. (2006). Comparative Characterization of the Microelement Composition of Kidney Stones from Patients in the Novosibirsk and Omsk Regions. *Chemistry for sustainable development*, 15 (2007) 55p61
- Hesse, A. (2009). Urinary tract stones. In F. Lang (Ed.), *Encyclopedia of molecular mechanisms of disease*. Berlin: Springer. (pp. 2144–2147).
- Hesse, A., and Sanders, G. (1988). *Atlas of infrared spectra for the analysis of urinary concrements* Stuttgart, 192.
- Japlaghi, M., Gholam Ali Fard, M. and Shayesteh, K. (2017). Monitoring and analysis of the land pattern of Lorestan province and the process of its change in the environment of GIS, *J. Nat Envi.*, (1)70, 15-35.
- Lai, H. C., Chang, S. N., Lin, H. C., Hsu, Y. L., Wei, H. M., Kuo, C. C. and Chiang, H. Y. (2019). Association between urine pH and common uropathogens in children with urinary tract infections. *Journal of Microbiology, Immunology and Infection* Volume 54, Issue 2, April 2021, Pages 290-298
- Joost. J. and Tessadri. R. (1986). Trace element investigations in kidney stone patients. *Euro. urol.*, 13(4), p: 264-270.
- Khattech. I. and Jemal. M. (1997). A complete solid-solution exists between Ca and Sr in synthetic apatite. *Thermochim Acta*, 298, 23.
- Keshavarzi, B., Yavarashayeri, N., Irani, D., Moore, F., Zarasvandi, A. and Salari, M. (2015). Trace elements in urinary tract stones: A preliminary investigation in Fars Province, Iran. *Envi. geoch and heal.*, 37(2), 377–389.
- Kohri, K., Garside, J. and Blacklock, N. (1988). The role of magnesium in calcium oxalate urolithiasis. *Bri. J. Uro.*, 61(2), 107–115.
- Kuta, J., Macha't, J., Benova', D., C ˇervenka, R. and Kor'istkova', T. (2012). Urinary calculi—atypical source of information on mercury in human biomonitoring. *Cent. Eur.*

- J. Chem.*, 10(5), 1475–1483.
- Lohiya, A., Kant, S., Kapil, A., Gupta, S. K., Misra, P. and Rai, S. K. (2017). Population-based estimate of urinary tract stones from Ballabgarh, northern India. *Nat. med. J Ind.*, 30(4), 198.
- McGrath, K. M. (2001). Probing material formation in the presence of organic and biological molecules. *Adv. Mat.*, 13(12-13), 989-992.
- Meyer, J. L. and Thomas, Jr. W. C. (1982). Trace metal-citric acid complexes as inhibitors of calcification and crystal growth. II. Effects of Fe (III), Cr (III) and Al (III) complexes on calcium oxalate crystal growth. *J. urol.*, 128(6), 1376-1378.
- Munoz, J. A., and Valiente, M. (2005). Effects of trace metals on the inhibition of calcium oxalate crystallization. *Urol. Res.*, 33(4), 267–272.
- Perk, H, Ahmet Serel, T., Kosar, A., Deniz, N. and Sayin, A. (2002). Analysis of the trace element contents of inner nucleus and outer crust parts of urinary calculi. *Urol Int* 2002;68:286–290
- Rani, L., Thapa, K., Kanojia, N., Sharma, N., Singh, S., Grewal, A. S. and Kaushal, J. (2020). An extensive review on the consequences of chemical pesticides on human health and environment. *J. Cl. Pro.*, 124657.
- Robertson, W. G. Peacock, M. Heyburn, P. and Hanes, F. (1980). Epidemionological risk factors in calcium stone Disease. *Scan. J. Uro and Nep.*, 53, pp. 15–28.
- Safarinejad, M. R. (2007). Adult urolithiasis in a population-based study in Iran: prevalence, incidence, and associated risk factors. *Urol. Res.*, 35(2), 73–82.
- Siener, R., Jahnen1, A. and Hesse, A., (2004). Influence of a mineral water rich in calcium, magnesium and bicarbonate on urine composition and the risk of calcium oxalate crystallization, *Eur. J. Cli. Nutr.*, 58: 270-276.
- Touryan, L. A. Lochhead, M. J. Marquardt, B. J. and Vogel, V. (2004). Sequential switch of biomineral crystal morphology using trivalent ions. *Nat Mat.*, 3(4), pp. 239–243.
- Wang, P., Zhang, H., Zhou, J., Jin, S., Liu, C., Yang, B. and Cui, L. (2021). Study of risk factor of urinary calculi according to the association between stone composition with urine component. *Sci rep.*, 11(1), 1-7.
- Wang, S., Zhang, Y., Zhang, X., Tang, Y. and Li, J. (2019). Upper urinary tract stone compositions: the role of age and gender. *Int braz.j urol.*, 46, 70-80.
- Yavar Ashayeri, N, Keshavarzi, B, Zarasvandi, A. and Mor, F. (2014). Geochemistry of urinary tract stones as one of the harmful biominerals: a case study of Fars province, *J. Adv. Ap. Geo.*, 13, 50-42.
- Zarasvandi, A., Carranza, E. J. M., Heidari, M. and Mousapour, E. (2014). Environmental factors of urinary tract stones mineralogy, Khouzeestan Province, Iran. *J. Afr. Eart. Sci.*, 97, 368–376.
- Zarasvandi, A., Heidari, M., Sadeghi, M. and Mousapoor, E. (2013). Major and trace element composition of urinary tract stones, Khuzestan province, Southwest, Iran. *Journal of Geochemical Exploration*, 131, 52–58.