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Chemical analysis of brown meager (*Sciaena umbra*) cephalides and traditional medicinal usage in urolithiasis

Sciaena umbra sefalitlerinin kimyasal analizi ve ürolitiaziste yerel bir tedavi yöntemi olarak uygulanması

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Öz

Giriş: Üriner sistem taş hastalıklarının yöresel yöntemlerle tedavisinde bölgesel farklılıklar bulunmaktadır. Doğu Karadeniz bölgesinde denizde göç etmeyen yerli bir balık olan eşkina (*Sciaena umbra*)'dan elde edilen sefalitler yöresel olarak *nefrolitiazis* tedavisinde yararlanılmaktadır. Diyet içeriğinde bulunan elementler *nefrolitiazis* patogenezinde önemli rol oynamaktadır. Sunulan araştırmada S.umbra'nın sefalitelerinin halk arasında ürolitiazis tedavisinde kullanımı tartışılmaktadır. Gereç ve Yöntem: *S. umbra* sefalitlerinin halk arası kullanımı yerel halktan sorgulandı. Sefalitlerin mineralojik ve kimyasal analizleri X- Işını difraktometre ve "inductively coupled plasma optical emission spectroscopy" (ICP–OES) yöntemi ile yapıldı. Halkın *S. umbra* sefalitlerini limon (Citrus limon) ile birlikte kullandığı saptanmıştır. Halkın kullanım şekline göre; 15 adet balık kafatası anterior dan ayrılmaktadır. İntrakranial kısımda orbita çukurunun posteriorunda kalan sefalitler çıkarılır. Elde edilen 30 adet materyal, 500 gr'lık kavanoz içinde ezilerek, üzerlerini örtecek kadar taze hazırlanmış limon (Citrus limon L.) suyu ilave edilmektedir. Bu karışım ışık geçirmeyecek şekilde alimünyum folyo ile kaplanmaktadır. Bu karışım içinde eriyerek oluşan karışımı hastaların yaklaşık 30 gün içinde tükettiği öğrenilmiştir. Canlının daha çok Eylül ile Kasım ayları arasında yakalandığı öğrenilmiştir. Elde edilen materyalin kullanım süre sınırı bulunmamaktadır. Sefalitlerin kalsiyum karbonat (CaCO3) bileşik konsantrasyonu en yüksek içeriğe sahiptir. Yapısal olarak aragonit ağırlıklıdır, magnezyum (Mg) oranı 4883,16 (ppm) yüksektir. Ana bileşen kalsiyum (Ca) dur. Sonuç: *Nefrolitiazis* patogenezinde diyet ile alınan sitrat ve magnezyumun etkisi olması nedeni ile karışımın içerdiği yüksek yoğunluktaki mineral varlığı *nefrolitiazis* oluşumda önemlidir. Kısa sürede yüksek miktarda sitrat ve bununla birlikte magnezyum alımının; taş çapının değişimine etkisi ve spontan taş düşürmeye yardımcı olduğu, bunun bir sonucu olarak da folklorik kullanımda önem kazandığı düşünülmüştür. Tartışma:Geleneklerin kısa zamanda oluşmadığı düşünülürse, folklorik olarak kullanılan yolların, kimyasal analizlerle eşliğinde ileri değerlendirme ve çalışmalara ihtiyaç olduğu söylenebilir.

Anahtar Kelimeler: *Nefrolitiazis*, geleneksel tıp, *Sciaena umbra*, sefalit, aragonit, kalsiyum.

Abstract

Introduction: There are regional differences in the treatment of urinary system stone diseases via local methods. In the Eastern Black Sea region; cephalides obtained from a domestic fish called brown meager (*Sciaena umbra*) that does not migrate in the sea, are regionally utilized in the treatment of *nephrolithiasis*. Elements in the diet play an important role in pathogenesis of *nephrolithiasis*. In the submitted research; the usage of cephalides of *S. umbra* in the treatment of urolithiasis is investigated. Materials and Methods: Regional usage of *S. umbra* cephalides was queried amongst the local community. Mineralogical and chemical analysis of cephalides were performed by the X-ray diffractometer and "inductively coupled plasma optical emission spectroscopy"

(ICP–OES) methods. It was observed that the community is using *S. umbra* cephalides together with lemon (*Citrus x limon*). According to the community's way of usage; 15 fish skulls were separated from the anterior. Cephalides in posterior of the orbital socket in the intracranial section were removed. 30 units were obtained, crushed in a 500 gr jar and fresh prepared lemon (*Citrus x limon*) juice was added in order to cover them. This mixture was covered with an aluminum foil to make it light-proof. It was learnt that the product that is solved in this mixture is consumed by the patients approximately within 30 days. It is known that *Sciaena umbra* is mostly caught between September and November. The obtained material obtained has no time limit for usage. *Calcium carbonate* (CaCO3) compound concentration of cephalides has the highest content. It is structurally aragonite-based and the magnesium (Mg) ratio is as high as 4883.16 (ppm). The main component is calcium (Ca). Results: Due to the efficiency of citrate and magnesium that are taken together with the diet in *nephrolithiasis* pathogenesis; the presence of a high-density mineral is important in the formation of *nephrolithiasis*. It is suggested that citrate and magnesium intake in a short period of time has supported the change in the stone diameter and spontaneous stone passingas a result of this. Thus, it has gained importance in folkloric usage. Discussion: Considering that traditions do not form in a short time; it can be specified that folkloric ways need further evaluations and studies accompanied by chemical analyses.

Keywords: *Nephrolithiasis*, traditional medicine, *Sciaena umbra*, cephalide, aragonite, calcium.

Introduction

Urinary system stone disease is one of the oldest known diseases. It was reported that a urinary system stone was found in the pelvic region of a young man in a grave close to El-Amrah (Egypt) and dated 4800 BC (1). Reports about the first stone analysis were prepared in the later 18th century (1). For this disease with historical importance; there are outstanding treatment forms of every culture and different geographies some of which leads regionally while some are found throughout the world. As the Eastern Black Sea region has a rich flora and fauna since the ancient periods; there are also folkloric applications regarding *nephrolithiasis*.

Brown meagre (*Sciaena umbra*) fish from sciaena family which generally lives in the Marmara Sea and the Black Sea has two white bone stones behind its eyes and over the brain. Some people drink the solution of these stones dissolved in natural lemon juice and olive oil in order to extract or reduce their kidney stones without surgical operation. Dusts of these samples are commercially available and they are used for diseases with stones in human kidneys and urinary tracts (2).

Sciaena umbra is a fish from *Sciaenidae* family that does not migrate and lives throughout the coasts of Turkey, Bulgaria, Romania and Caucasus (3). This organism is called as umbra, brown meager or shi drum by the community. Similarly, *Umbrina cirrosa* from the same family is defined as umbra and coranicus chialcis, and cephalides of these organisms are also used by the community with the same application form. Although they are used for regional treatments with different purposes in different cities of the region; the main usage of cephalides is aimed at passing stones in urolithiasis.

In the presented research; the place of *Sciaena umbra* within traditional treatment methods in Turkey, and the chemical analysis of cephalides obtained from this organism will be discussed.

Materials and Methods

The research was executed in the Eastern Black Sea region. Upon getting information about the methods that were used in stone passing treatment and that were successful from the anamnesis of the patients who had visited Hopa State Hospital with urinary stone complaints; folkloric treatment methods were recorded. *S. umbra* cephalides used to eliminate the complaints of the patients who visited were obtained from the *S. umbra* fish that were commercially sold after being caught in the Eastern Black Sea region where the community obtains its supplies.

S. umbra cephalides were taken to mineralogical and chemical analysis at Süleyman Demirel University's Geothermal Energy, Groundwater and Mineral Resources Research and Application Center. *S. umbra* cephalide was powdered by milling at 40 micron. This powder sample was taken to analysis between 10 and 750 scanning range. X-Ray diffractometer (by Panalytical brand PW3040/X'Pert Pro model XRD device) anode Material: Cu (Kα1.54060), divergence Slit Size [0]: 0.9570, receiving Slit Size [mm]: 0.2000, generator settings: 40 mA 45 Kv, step size [02Th]: 0.0200, soller Slit: 0.04 rad. Parameters were used. Chemical analysis of *S. umbra* cephalide was

performed by Perkin Elmer ICP-OES device.

Results

It was observed that the community is using *S. umbra* cephalides together with lemon (*Citrus ˣ limon*). According to the usage method of the community; 15 fish skulls were separated from the anterior. Cephalides in posterior of the orbital socket in the intracranial section were removed. 30 units were obtained, crushed in a 500 gr jar and fresh prepared lemon (*Citrus ˣ limon*) juice was added in order to cover them. This mixture was covered with an aluminum foil in order to make it light-proof. It was learnt that the product that is solved in this mixture is consumed by the patients approximately within 30 days. It was found out that viable specimens are mostly caught between September and November months. The obtained material has no time limit for usage. X-ray diffractometer 10-750 scanning results of *Sciaena umbra* cephalide is given in Figure-1.

Concentration of *calcium carbonate* (CaCO3) was high and 20.51% of its chemical content was calcium. Chemical analysis results are given in Table 1.Table 1: Biochemical analysis of *Sciaena umbra* cephalides 2Θ peak values in the scanning of *S. umbra* sample and 2Θ peak values in XRD device mineral card were compared. 2Θ peak values in the scanning of *S. umbra* cephalide sample complied with the peak values in the *calcium carbonate* mineral card (4). 2Θ values in the *S. umbra* cephalide sample scanning were 25.49, 26.51 and 36.37 respectively and they conformed to the peak values in the aragonite mineral card (5).

Conclusion and Discussion

Although herbal treatments are preferred in the world; products with animal origins are also traditionally used for treatment purposes. According to the study by Ortiz-Alvarado, who investigated the use of fish oil in the dietary management of hypercalciuric stone

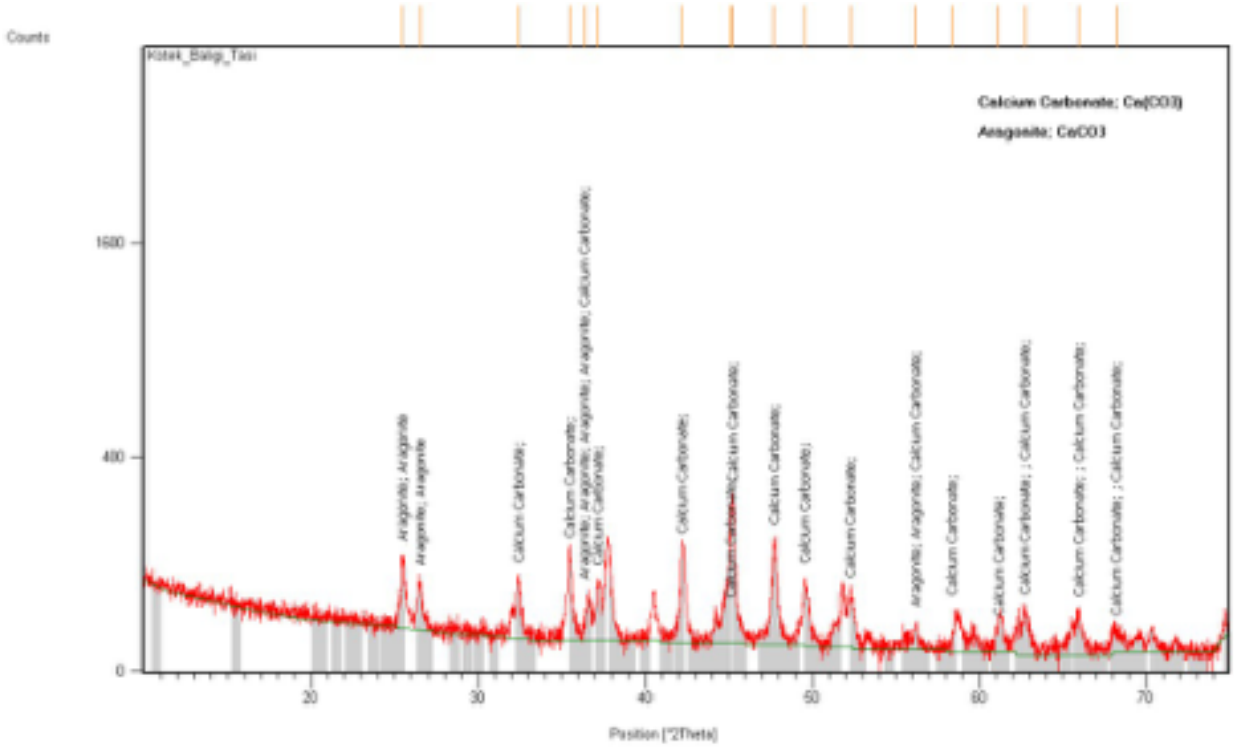

Figure 1: *X- ray diffractometer of Sciaena umbra cephalides*

Table 1: Biochemical analysis of *Sciaena umbra* cephalides

	Mg (ppm)	Fe (ppm)	Zn (ppm)	Cd (ppm)	Pb (ppm)	Cu (ppm)	Cr (ppm)
Sciaena umbra cephalides	4883,16	9,41	8,30	<0,1	<0,1	6,64	<0,1

*ppm: Parts per million

formers, Prostaglandins were linked to urinary calcium excretion, suggesting a role for omega-3 fatty acids in the treatment of hypercalciuric urolithiasis. According to the same study, Omega-3 fatty acids combined with empiric dietary counseling resulted in a measurable decrease in urinary calcium and oxalate excretion and an increase in urinary citrate in hypercalciuric stone formers (6). According to the study of Lev (7) where he specified the traditional treatments of Levantines (person who is of European descent and a resident in Near East and whose breed is mixed by marriages (8)) according to specific periods, he has specified that *Pediculus sp* (phthirus), *Sepia officinalis* (cuttle fish) and *Cimex lectularius* (bed bug) have been used for the treatment of urinary tract obstructions, *Capra hircus* (goat), *Lampyris sp* and *Chlamydotis undulata* (Houbara) have been used for the treatment of kidney stones, *Vivera civetta* (Civet cat), *C.hircus* and *Titurus vittatus* (amphibious triton) have been used for increasing sexual functions and as an aphrodisiac, *Corvus corax* (raven) has been used for impotency, and *Erosaria sp*. (sea shell) have been used for the treatment of gonorrhea (7). In the study of Tefekli et al.; they specified the stone frequency in the Black Sea region as 14.3% (9). Herbal treatment use is also present in the region. According to Yaldız et al.; *Digitalis lamarckii Ivan* (*Scrophulariaceae*; local name: East fox glove), *Colchicum autumnale L.* (*Liliacea*; local names: Meadow Saffron, Autumn crocus, Vargit, Kalkgit) have been used for kidney diseases (10).

Aragonite structure is another polymorphous formation that is very similar to the calcite structure of *calcium carbonate* in organisms that can perform mineralization (11). In recent studies; it was found that high magnesium in the sea water had no effect on aragonite structure and it suppressed calcite formation. It was also stated that the magnesium ratio was active in this case and it triggered soluble magnesium calcite structure instead of pure calcite formation (12).

Another study pointed out that, concentration of CaCO3 compound in the sample was high range. As it can be seen in Figure 2, XRD data for aragonite peak values in the figure were compared with the 2 theta values. The main diffraction peaks of *calcium carbonate* (aragonite) at approximately 2θ = 26.2, 27.5 and 33.5 were in good agreement with the reference pattern of *calcium carbonate* (aragonite) given in the literature (JCPDS 24-0025) (2).

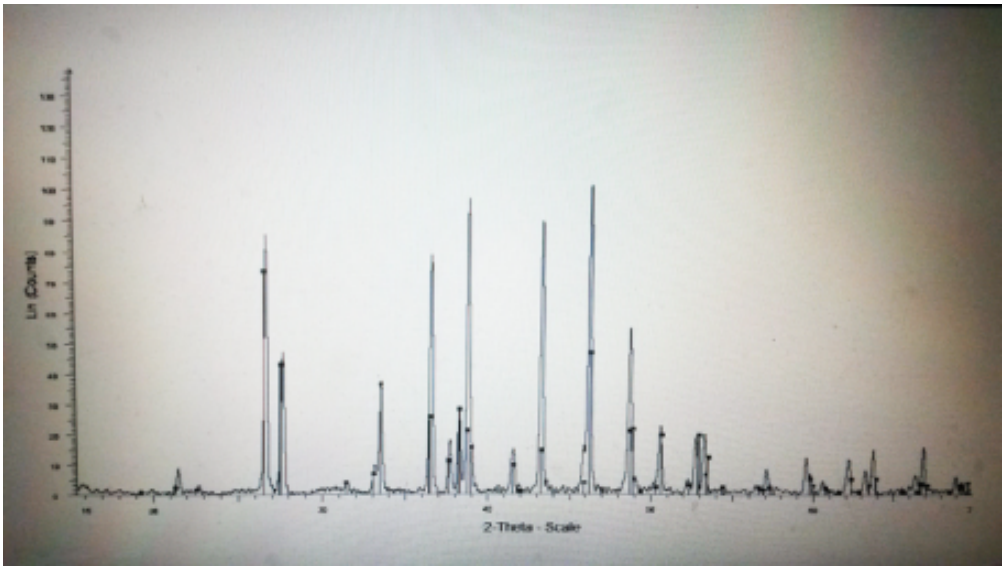

Figure 2 X-ray diffraction pattern of a bone stone of *Sciaena umbra* Fish sample

Fish get their mineral materials required for the formation of their osteoid structures and some of their physiological functions from their aquatic environment and the nutrients they take in. Among these mineral materials; especially calcium and magnesium are essential elements for the skeleton structure and the scales, and they have an important role in muscle contraction, blood clotting, transfer of neural stimuli, integrity of the cell membrane, and activation of various enzymes. When the calcium and magnesium demand of the fish is not met; anomalies in the skeleton and deficient mineralization in the osseous structure are observed (13). Measurement of the magnesium quantity in the sea water may explain the formation of aragonite form instead of calcites in sea organisms.

As a result of analysis; it was observed that the mineral was predominantly *calcium carbonate* (CaCO3) in the aragonite formation. In addition to calcium (Ca); the magnesium (Mg) amount was also higher when compared to other minerals.

As specified by Folk; morphology of *calcium carbonate* crystals are formed according to the crystallization ratio and the sodium (Na) and magnesium (Mg) content in the depositing water.[12] Magnesium selectively inhibits the formation of calcite structure. In this case; *calcium carbonate* (CaCO3) crystallization was followed in the aragonite structure. *Calcium carbonate* crystallization in the sediments that form in Mg-rich environments (ex. Beaches and ocean floor) is present in the aragonite structure. When sea water is evaporated; Mg/Ca ratio changes from 3:1 to 1:3 and an irregular crystallization structure develops (14). When the aragonite formation type is considered, it is suggested that biological CaCO3 sediment in the sea organism is a similar mechanism that can be seen in the aragonite structure.

There are no previous chemical or clinical studies regarding this material and its usage form. However, it is known that the materials in its content (citrate, Mg, Ca) have a place in the pathophysiology and treatment of urinary system stone diseases. Oster mentioned that citrate is an important naturally occuring inhibitor which inhibits calcium stone formation in urine (15). In a study performed with children having a ketogenic diet; McNally et al. reported that beneficial results with potassium citrate treatment were obtained in kidney stones (16). In a study of Resnick et al. about magnesium excretion and calcium oxalate stones; they have specified that magnesium inhibits calcium oxalate crystallization (17). According to a study Zerwekh et al. about potassium citrate; although an increase was observed in the calcium concentration in urea; saturation of calcium oxalate was relatively decreased due to the chelation of citrate and oxalate (18). In a study of Liebman et al. about oxalate absorption of magnesium and calcium; it was indicated that urine oxalate-calcium oxalate saturation and calcium oxalate crystals were important keys in the formation of the kidney stones (19). In the same study; it was also reported that oxalate absorption in the *calcium carbonate* and magnesium oxide treatment areas was lower when compared to the control group and it was almost effective as calcium in decreasing the magnesium oxalate absorption and urinary excretion (19). In a study of Taylor et al.; it was suggested that increase in the age and decrease of magnesium intake formed a risk for asymptomatic *nephrolithiasis* (20).

In the study of Hesse et al.; it was specified that aragonite structure was present within the components that are rarely found in the spectroscopic analysis of urinary stones (21).

In a study of Gault et al. about urinary system stones; they have mentioned that they encounter the *calcium carbonate* aragonite crystal form (22).

When the studies about traditional treatments are inspected; Christopher reports that otoliths have previously been used in treatment of various diseases including urinary problems, especially kidney and gall bladder stones, malaria, jaundice, fever, liver complaints and nose bleeding (23). Fish otoliths are still being used in the treatment of urinary system infections, protection against fever and insect stings. As an example; it is mentioned that fish otoliths are used for urinary tract infections in Turkey, for back pain and asthma in Brazil and for fever in Spain (23). It is also specified that *Sciaena Umbra* is used for urinary system infections (23). Moreover, Christopher refers to similar applications in different communities. It is specified that otoliths of the fish called *Micropogonias furnieri* (*Sciaenidae*; Local name: Whitemouth croaker) are consumed by

Brazilians for urinary problems as tea after boiling, while they were also used for the treatment of kidney stones in 17th century (23). Additionaly, it is mentioned that otolith obtained from Tiburones in the Indian sea is used for the treatment of gall bladder stones (23).

According to the resources; instead of cephalides, egg shells are used in the Central Anatolia region of Turkey and they are consumed after being mixed with fresh olive oil (24). However, it is observed that this way of treatment is not as common as the usage of *S. umbra* cephalides.

As herbal medicine treatment Dolichos biflorus and Orthosiphon grandiflorus in the prevention of urolithiasis and fish stone as a method of stone expulsion, the treatment effect and mechanism of action remains to be elucidated yet (25).

As a result of the chemical analyses performed; no direct correlation was found between the reasons of usage by the community and the crystal structure and element quantity within the otoliths. The relationship between citrate and magnesium inside the mixture with the pathophysiology of *nephrolithiasis* has been shown in numerous studies (15-20). As a hypothesis; it can be foreseen that receiving high quantities of citrate and relatively magnesium in a short period of time will help minimize the diameter of the stone and help spontaneously pass the stone in combination with hydration.

When it is considered that the traditions are not developed within a short period of time and that ongoing beliefs and usages for many centuries are taken into account, further evaluations and studies are required for all the methods used in traditional medicine, in addition to chemical analyses.

There is no conflict of interest between the authors.

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