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Original article

A Preliminary Investigation of *Lapis Judaicus* as a Natural Anti-Nephrolithic Agent: Physicochemical Characterization and Pilot *in vivo* Study in Albino Mice

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Abstract
Kidney stones represent a significant global health burden, with calcium oxalate stones accounting for approximately 80% of all cases. Traditional medicine systems have long utilized natural remedies for urolithiasis management, among which *Lapis Judaicus* (Hajar al-Yahood) holds a prominent position in Unani and Middle Eastern medicine. This preliminary experimental study investigated the litholytic potential of *Lapis Judaicus* using two distinct natural vehicles: lemon juice and yogurt. Four groups of male albino mice were employed: one healthy control, one nephrolithiasis group induced by calcium oxalate (80 mg/kg) over four consecutive days, and two treatment groups orally administered *Lapis Judaicus* (250 mg/kg) suspended in either lemon juice or yogurt for six days. Histopathological examination revealed complete dissolution of kidney stones and restoration of normal renal architecture in the mice treated with *Lapis Judaicus* in lemon juice, whereas the yogurt-treated group showed partial improvement with a noticeable reduction in stone size and number. Interestingly, although prior solubility tests indicated superior dissolution of *Lapis Judaicus* under acidic conditions (49.83% at pH 3.0), the acidic lemon juice vehicle demonstrated remarkable in vivo efficacy, suggesting the involvement of additional biological or chemical synergistic factors. These findings provide preliminary support for the traditional use of *Lapis Judaicus* in kidney stone management and highlight the potential of citrus-based delivery systems to enhance its litholytic activity. Further comprehensive studies are crucial to elucidate the precise mechanisms of action, optimize therapeutic dosing regimens, and establish safety profiles for potential clinical applications.
Keywords. *Lapis Judaicus*, Hajar Al-Yahood, Nephrolithiasis, Calcium Oxalate.

Introduction

Nephrolithiasis, commonly known as kidney stone disease, affects approximately 12% of the global population and represents one of the most prevalent urological disorders worldwide [1,2]. The recurrence rate following initial stone formation ranges from 50% to 70% within ten years, imposing substantial economic and health problems on affected individuals and healthcare systems [3]. Among the various types of kidney stones, calcium oxalate stones constitute the predominant form, accounting for nearly 80% of all cases, followed by uric acid stones (5-10%), struvite stones (10-15%), and the relatively rare cystine stones (<1%) [4,5].

Lapis Judaicus, known in Arabic as "Hajar al-Yahood" (literally translated as "stone of the Jews"), represents a fascinating example of such traditional remedies. This naturally occurring mineral substance has been extensively documented in classical Unani medical literature, with one of the earliest references appearing in Kitab al-Hasha'ish, the famous herbal collection authored by Dioscorides in the first century AD [6]. From a therapeutic perspective, traditional Unani sources have historically prescribed *Lapis Judaicus* for managing various urological conditions, including renal calculi, dysuria, anuria, and urinary retention. *Lapis Judaicus* is often used in both single and compound formulations. It includes Unani preparations such as Majoon Hajrul Yahood and Kushta Hajrul Yahood, which are designed to dissolve kidney stones and promote their expulsion through the urinary tract [7,8]. Despite extensive historical use and anecdotal reports, there remains a knowledge gap concerning standardized preparation methods, pharmacodynamics, and clinical outcomes [9].

Recent scientific investigations have begun to validate these traditional applications through controlled experimental studies. A notable randomized, double-blind clinical trial conducted by Faridi and colleagues in 2014 demonstrated that oral administration of *Lapis Judaicus* powder significantly reduced the size of calcium-based kidney stones in human subjects [7]. The study further reported favorable biochemical changes, including a reduction in urinary calcium levels and an increase in urinary magnesium, without significant adverse effects. These clinical outcomes have been documented by preclinical investigations, such as the study by Khoshnoud and colleagues in 2023, which utilized an ethylene glycol-induced urolithiasis rat model [10]. Treatment with *Lapis Judaicus* significantly inhibited stone formation, reduced serum blood urea nitrogen levels, and improved several urinary parameters, including increased urinary citrate and pH, along with reductions in urinary protein, calcium, oxalate, and phosphorus levels [11].

Despite these promising preliminary findings, significant gaps remain in our understanding of the chemical composition, mechanism of action, and optimal delivery systems for *Lapis Judaicus*. The present study was

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therefore designed to address several research questions: First, to characterize the physical and chemical composition of *Lapis Judaicus* samples obtained from local Libyan markets using advanced analytical techniques. Second, to evaluate its litholytic efficacy in an experimentally induced calcium oxalate nephrolithiasis model in albino mice. Third, to compare the therapeutic effectiveness of two traditionally used delivery vehicles: lemon juice and yogurt, in enhancing the bioavailability and therapeutic action of *Lapis Judaicus*. By integrating ethnopharmacological survey data, comprehensive physicochemical characterization, and controlled in vivo experimentation, this research aims to provide a scientifically rigorous evaluation of this traditional remedy and contribute to the growing body of evidence supporting the potential role of natural products in nephrolithiasis management.

Materials and Methods

The study employed a systematic approach to assess the lithotriptic potential of *Lapis Judaicus* through ethnobotanical surveys, chemical analyses, and controlled in vivo experiments using albino mice.

Ethnobotanical Survey

A structured ethnopharmacological survey was conducted among eighteen traditional herbalists in Tripoli, Libya. Practitioners were selected from different districts for their documented experience with mineral-based remedies. A comprehensive questionnaire systematically collected data on user demographics, preparation methods (powder with water, lemon juice, or yogurt), and traditional therapeutic claims.

Sample Collection and Authentication

Lapis Judaicus specimens were obtained from several herbalists and mineral vendors in Tripoli. Samples marketed as "Hajar al-Yahood" were visually authenticated for characteristic morphological features following WHO guidelines [12]. Authenticated samples were cleaned, dried, and stored under controlled conditions before analysis.

Physicochemical Characterization

XRF Analysis: Elemental composition was determined using X-ray fluorescence spectrophotometry. Finely ground samples were analyzed for major and trace elements following standard protocols [13].
FTIR Spectroscopy: Functional groups were identified using Fourier-transform infrared spectroscopy. Samples mixed with KBr (1:100 ratio) were analyzed across a 4000-400 cm^{-1} wavelength range [14].
Dissolution Testing: Samples (1.0 g) were immersed in 50 mL of three media: distilled water (pH 7.0), 0.1N HCl (pH 3.0), and 0.1N NaOH (pH 10.0). Dissolution rates were recorded over 24 hours at room temperature with continuous stirring.

Preparation of Lapis Judaicus formulations

Lapis Judaicus was prepared as in folk use in Libya, finely powdered using a mortar and pestle before use. For oral administration, two different formulations were prepared each day, freshly.
For the lemon juice formulation, 250 mg of powdered *Lapis Judaicus* was dissolved in 10 mL of lemon solution consisting of 5 mL freshly squeezed lemon juice and 5 mL distilled water, yielding a final concentration of 25 mg/mL. The solution was shaken vigorously immediately before administration to ensure homogeneity. For the yogurt formulation, 250 mg of powdered *Lapis Judaicus* was suspended in 10 mL of yogurt solution composed of 5 mL commercial plain yogurt from Alnaseem, Misurata, Libya. and 5 mL distilled water, resulting in a final concentration of 25 mg/mL. The suspension was thoroughly mixed prior to each oral gavage to maintain uniform dispersion. Both preparations were administered orally at the required dose based on body weight.

Laboratory Animals

Twenty-four male Swiss albino mice (body weight 25 ± 5 g) were obtained and acclimatized for one week prior to experimentation. Animals were housed in standard polypropylene cages under controlled laboratory conditions. All experimental procedures were conducted in accordance with internationally accepted guidelines for the care and use of laboratory animals.

Chemicals and reagents

All chemicals were of analytical grade and purchased from MERCK (E. Merck, F.R. Germany) and (BDH Chemicals Ltd., Poole, England).

Experimental Design

The animals were randomly divided into four groups (n = 6 per group). Group I (normal control) received normal saline (5 mL/kg, orally) throughout the experimental period. Nephrolithiasis was induced in Groups II–IV by intraperitoneal administration of calcium oxalate (CaOx) at a dose of 80 mg/kg once daily for four consecutive days. Group II served as the disease control and received no further treatment following induction. After a 24-h post-induction period, Groups III and IV were treated with *Lapis Judaicus* at a dose

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of 250 mg/kg/day by oral gavage for six consecutive days. The formulation was administered as a solution prepared in lemon juice for Group III and as a suspension prepared in yogurt for Group IV.

Histopathological Analysis

At the end of the treatment period, animals in each group were sacrificed, and the kidneys were excised and rinsed with normal saline. The specimens were cut into small pieces and fixed in 10% neutral buffered formalin. For histopathological evaluation, the tissues were processed in a histopathology laboratory, embedded in paraffin wax, and sectioned at a thickness of 5 µm using a microtome. The paraffin was removed, and the sections were mounted on glass slides and stained with hematoxylin and eosin (H&E) according to standard procedures [15]. The stained sections were examined under a light microscope for histopathological analysis.

Results

Ethnobotanical Survey

The survey conducted among herbalists in Tripoli confirmed that herbal remedies are a primary traditional method for treating kidney stones in Libya. While several plants were identified, including *Euphorbia Spp.* (Rabbit Herb), *Acacia Senegal* (Arabic Gum), Parsley Seeds, and *Lapis Judaicus* were found to be the most trusted and frequently mentioned remedies. Lemon juice was the most common vehicle (72%), followed by yogurt (20%) and water (8%) (Figure 1). Furthermore, the age group most frequently utilizing these remedies is 20–40 years old, followed by the 40–60 group.

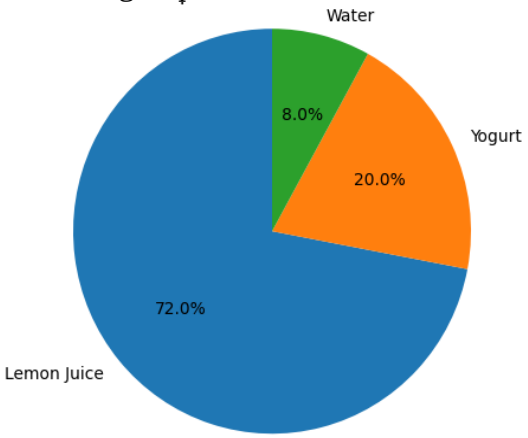

Figure 1. Traditional preparation methods reported by herbalists (n = 18)

Physicochemical Characterization

XRF Results: Chemical analysis revealed that the sample is predominantly composed of calcium (50.51%) and carbonate (46.6% as CO_2 loss on ignition), confirming a high-purity calcium carbonate material (Table 1). Minor constituents included magnesium (0.705%), iron (0.635%), and silicon (0.560%). The combined Ca and CO_2 content (97.11%) is consistent with calcite ($CaCO_3$) as the primary mineral phase. Minor constituents (Mg, Si, Fe) bring the total elemental content to 98.01%, corroborating the FTIR findings.

Table 1. X-Ray Fluorescence (XRF) Spectroscopy Analysis of Lapis Judaicus

Element	Percentage (%)
Calcium (Ca)	50.51
L.O.I (as CO_2)	46.6
Magnesium (Mg)	0.705
Silicon (Si)	0.560
Iron (Fe)	0.635
Total	98.01

FTIR Results: FTIR analysis revealed characteristic absorption bands indicating the mineral composition of the sample (Table 2). Calcium carbonate ($CaCO_3$) was identified by peaks at 712, 872.6, 1394, and 1797 cm^{-1}, corresponding to carbonate functional groups. A prominent band at 1030 cm^{-1} indicated the presence of montmorillonite clay mineral. Notably, the absence of absorption bands in the 2000-3500 cm^{-1} range confirmed no detectable organic materials (C-H stretching vibrations) in the sample.

Dissolution Results: Solubility tests demonstrated strong pH-dependent dissolution of *Lapis Judaicus* (Table 3). The sample exhibited maximum solubility in acidic conditions (49.83% at pH 3.0), consistent with the acid-labile nature of calcium carbonate. Solubility decreased dramatically at neutral (5.62% at pH 7.0) and alkaline (4.10% at pH 10.0) pH, confirming the material's stability under non-acidic conditions.

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Table 2. Fourier-Transform Infrared (FTIR) Spectroscopy Analysis of Lapis Judaicus

Wavenumber (cm^{-1})	Assignment	Functional Group/Mineral
712.0	$CaCO_3$	In-plane bending (ν_4)
872.6	$CaCO_3$	Out-of-plane bending (ν_2)
1030.0	Montmorillonite	Si-O stretching
1394.0	$CaCO_3$	Asymmetric stretching (ν_3)
1797.0	$CaCO_3$	Combination band
2000-3500	No peaks observed	Absence of organic C-H bonds

Table 3. pH-dependent solubility of Lapis Judaicus

pH Condition	Sample Weight (g)	Volume (mL)	Solubility (%)
pH 3 (Acidic)	1.0	50	49.83
pH 7 (Neutral)	1.0	50	5.62
pH 10 (Alkaline)	1.0	50	4.10

Histopathological Results

Histological examination of kidney sections in the normal control group revealed normal renal architecture. Renal corpuscles exhibited a normal urinary space, and tubular structures, including proximal and distal convoluted tubules as well as glomeruli, appeared histologically normal (Figure 2A). However, the calcium oxalate–treated group showed translucent oxalate crystals within the renal tubules. Cytoplasmic vacuolization with focal areas of tubular atrophy was observed among tubular epithelial cells, while the interstitial tissue showed sparse reactive lymphoid aggregates and numerous congested blood vessels of variable caliber (Figure 2B). In contrast, treatment with a lemon juice solution of *Lapis Judaicus* showed a surprisingly improved histological picture, leading to the almost complete disappearance of the induced oxalate crystals in all sections. The renal tissues demonstrated full recovery, with restoration of normal glomerular and tubular structures. No evidence of residual crystals, fibrosis, or inflammatory infiltrates was detected, validating the high efficacy of this traditional combination (Figure 2C). Only partial improvement was observed in the remaining treatment group (yogurt-treated). Although there was a noticeable reduction in the size and density of the crystals compared to the induction group, microscopic examination revealed that some intraluminal translucent oxalate crystals persisted within the renal tubules. This suggests that while the *Lapis Judaicus* possesses intrinsic litholytic properties, the choice of vehicle (yogurt) might retard its effect.

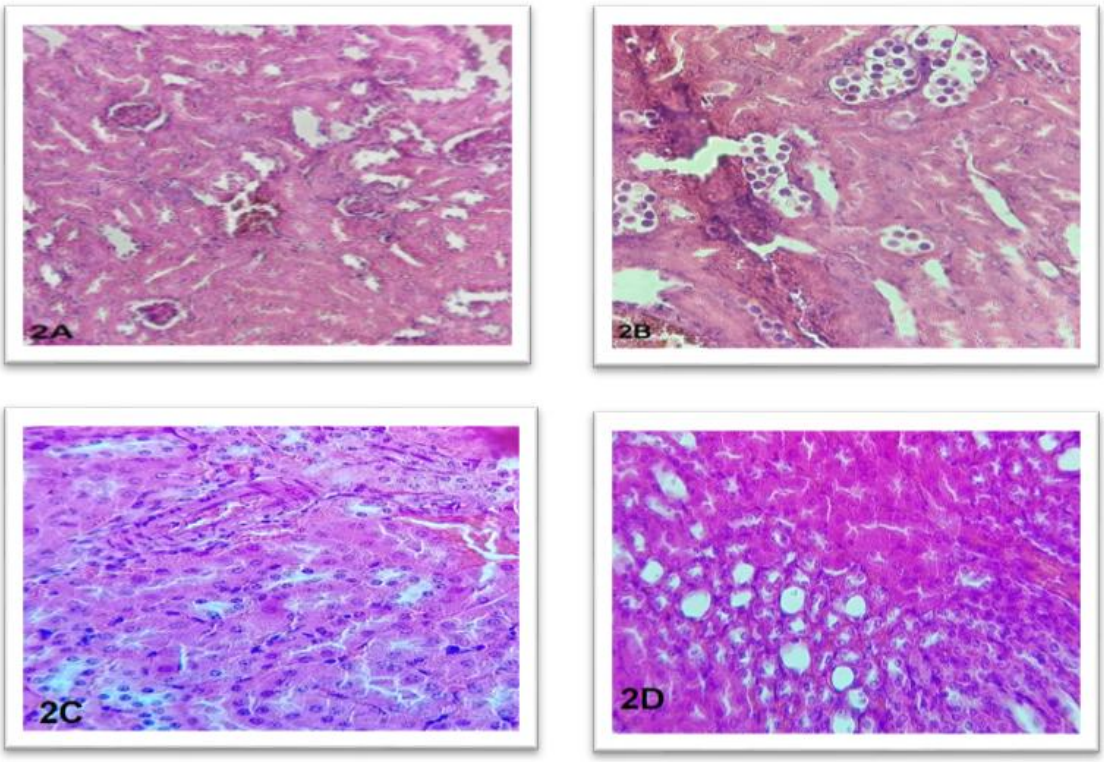

Figure 2. Photomicrographs of kidney tissues from different experimental groups. (2A) Normal control group showing normal renal architecture with intact glomeruli and tubules. (2B) Calcium oxalate–treated group showing intratubular oxalate crystals, tubular vacuolization, focal atrophy, mild interstitial inflammation, and vascular congestion. (2C) Lemon juice solution of Lapis judaicus–treated group showing near-complete disappearance of crystals with restoration of normal renal structure and no fibrosis or inflammation. (2D) Yogurt-treated group showing partial improvement with reduced crystals, although some intratubular crystals persist (H&E, 200×).

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Discussion

The current study suggests that *Lapis Judaicus* exhibits significant litholytic activity against calcium oxalate nephrolithiasis, with its efficacy strongly influenced by the delivery vehicle. The superior performance of the lemon juice vehicle compared to yogurt may be explained by the dissolution data, which demonstrated maximal solubility of *Lapis Judaicus* under acidic conditions. A previous experimental study reported that lemon juice alone may be beneficial in nephrolithiasis due to its high content of vitamin C, vitamin E, and citrate, which are thought to inhibit calcium oxalate crystal formation and attachment in the kidneys [16]. However, a small clinical trial involving 11 patients who consumed concentrated lemon juice daily for several years showed a reduction in stone formation that did not reach statistical significance [17].

In the present experiment, *Lapis Judaicus* administered in lemon juice resulted in marked histopathological improvement, with inhibition of calcium oxalate crystallization to a level comparable to normal renal tissue. One proposed mechanism, supported by molecular dynamic modeling, suggests that acidic pH enhances dissolution in the gastrointestinal tract, facilitating the release of bioactive minerals such as magnesium, which may competitively inhibit calcium oxalate crystal growth [18]. The minor silicon content may also contribute through antioxidant effects, consistent with a previous in vivo study demonstrating that selenium–silica nanospheres reduced calcium oxalate crystal deposition and attenuated oxidative renal damage [19].

Although yogurt is a source of dietary calcium and has been reported to reduce calcium oxalate stone risk by binding intestinal oxalate and decreasing its absorption, its use as a vehicle for *Lapis Judaicus* in the current study did not result in comparable histopathological improvement [20]. The ethnobotanical survey findings are consistent with the experimental data, as most herbal practitioners preferred lemon juice as the delivery vehicle, reflecting alignment between traditional practice and experimental evidence.

These findings extend previous human and animal studies, confirming the litholytic potential of *Lapis Judaicus* and identifying lemon juice as a more effective delivery system. Furthermore, XRF analysis showed that toxic heavy metals were not detected, supporting its potential safety for future clinical applications.

Limitations of The Study

Larger studies are needed to assess the independent effects of different delivery vehicles on nephrolithiasis outcomes with a comprehensive assessment of systemic and urinary biochemical parameters. Inclusion of both sexes with expanded sample sizes.

Conclusion

This preliminary experimental study suggests that *Lapis Judaicus* may possess potential litholytic activity in a calcium oxalate nephrolithiasis model in albino mice, with efficacy influenced by the delivery vehicle. Administration with a lemon juice vehicle demonstrated greater calcium oxalate kidney stone dissolution and improved histopathological features compared with the yogurt group. Physicochemical analysis identified calcium carbonate as the principal component, with no detectable toxic heavy metals, and enhanced solubility under acidic conditions.

Conflict of Interest Statement

The author declares no conflicts of interest related to this research.

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