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## Research Paper

Randomized and double-blinded clinical trial of the safety and calcium kidney stone dissolving efficacy of *Lapis judaicus*

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## ABSTRACT

**Ethnopharmacological relevance:** Kidney stones are one of the most common disorders of the urinary tract and cause a great deal of morbidity and economic loss. Because of the side effects and costs of current interventional procedures, researchers are interested in finding medicinal therapies. In this regard, some reports have focused on traditional medicines as a drug discovery resource. Iranian scholars in the medieval era recommended *Lapis judaicus* for the prevention and treatment of kidney stones. The present study assessed the efficacy and safety of *Lapis judaicus* on the size of calcium kidney stones and some related biochemical factors in blood and urine.

**Materials and methods:** Sixty patients with kidney stone disease were included in this double-blind randomized clinical study. Thirty patients received 2 g of *Lapis judaicus* powder in hard capsules per day for 10 weeks, and another 30 patients received a placebo for the same period. Ultrasonography was performed on patients, and blood and urine samples were collected before and after the study to evaluate the efficacy and safety of *Lapis judaicus* in calcium kidney stone patients.

**Results:** The size of the kidney stones was reduced significantly ( $p < 0.001$ ) in the drug group. In 9 patients from the drug group, the stone was completely dissolved. Moreover, urine calcium concentration and specific gravity were reduced and urine magnesium was increased ( $p < 0.05$ ). *Lapis judaicus* did not affect BUN, creatinine, ALT, or AST.

**Conclusion:** Contrary to the placebo group, the size of kidney stones was reduced significantly in the treatment group after oral administration of *Lapis judaicus*. This preliminary study confirms traditional knowledge of the efficacy and safety of *Lapis judaicus* in kidney stone diseases and suggests a new method to treat calcium kidney stones. Further detailed *in vitro* and *in vivo* studies aimed at discovering the mechanism of action of *Lapis judaicus* and clinical studies involving a larger population of patients will be necessary to fully explain and confirm the results obtained in the present study.

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## 1. Introduction

Kidney stone disease is a major clinical and economic burden for healthcare systems around the world. Calcium-containing kidney stones are >90% of all stones (Merchant et al., 2008; Okada et al., 2009). The current management of stone disease ranges from observation to surgical removal of the stone. Small stones (< 5 mm) are usually able to pass spontaneously, but larger

ones and stones that fail to pass should be treated by an interventional procedure such as extracorporeal shock wave lithotripsy, ureteroscopy, or percutaneous nephrolithotomy (Butterweck and Khan, 2009). The side effects and costs of current procedures have motivated researchers to find medicinal therapies (Coe and Asplin, 2010).

Iran has a long and prolific history in the practice and study of medicine. In the case of nephrology/urology disorders, Iranian medieval scholars did valuable work. Rhazes wrote a special book on urinary calculi in which he describes his methods for diagnosing and treating calculi (Ashtiyani and Cyrus, 2010). Avicenna dedicated a significant part of his encyclopedia "The Canon of Medicine" to kidney and bladder diseases and described in detail

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the fundamentals of treating kidney and bladder diseases, especially calculi (Faridi et al., 2012). In reviewing references of traditional Iranian medicine, we found that almost all Iranian physicians in the medieval era recommended *Lapis judaicus* for dissolving kidney stones (Faridi et al., 2013). Moreover, this traditional drug is still used to heal kidney stones in Iraq, Afghanistan (Hooper and Field, 1937), Jordan (Lev and Amar, 2002; Lev and Dolev, 2002), India, and Pakistan (Ali and Mahdihassan, 1984).

*Lapis judaicus* names the larger spines of regular echinoids, especially cidaroids such as *Balanocidaris glandifera* Munster, called Jews' stones (English); Sang-e-Jahudan (Persian), and Hajarul Yahud (Arabic). It was formed in the Late Jurassic (Oxfordian to Tithonian) period in Europe, North Africa, and the Middle East (Duffin, 2006).

Information about the pharmacological activity of *Lapis judaicus* is very limited. *In vivo* studies have shown that it has an inhibitory effect on the crystallization of calcium oxalate (Rao et al., 2008). Another study has shown that Qurs-e-Suzak (*Lapis judaicus* is one of its ingredients) has antimicrobial activities (Ahmed et al., 2009). Also Cystone<sup>®</sup>, a supplement for renal stones, contains *Lapis judaicus* (Mohanty et al., 2010). Recently, we reported that *Lapis judaicus* contains high concentrations of calcium, magnesium, and silicon and lower amounts of aluminum, sulfur, iron, potassium, and strontium (Faridi et al., 2013).

Considering the vast use of *Lapis judaicus* reported in traditional medicine and the preliminary *in vitro* and *in vivo* results, the present study assessed the safety and calcium kidney stone dissolving efficacy of *Lapis judaicus* as well as its effects on several related blood and urine biochemical factors.

## 2. Materials and methods

### 2.1. Drug and placebo preparation

*Lapis judaicus* was purchased from a local market in Shiraz, Iran. Fossils were identified by a paleontologist at the Department of Paleontology, Shiraz University and a voucher specimen deposited in the Shiraz School of Pharmacy collection (PM 499). Quality control tests including measurements of heavy metals and

microbial contamination were done based on United States pharmacopeia guidelines (Faridi et al., 2013). Physico-chemical assessments for the preparation of drug dosage forms were done as described previously (Faridi et al., 2013). White wheat flour was used for the placebo. One-gram capsules were prepared for both drug and placebo.

### 2.2. Clinical study

A double-blind randomized placebo-controlled clinical trial was performed to evaluate the safety and efficacy of *Lapis judaicus* capsules in calcium kidney stone patients.

#### 2.2.1. Ethical issues

The trial was conducted according to the guidelines of the Declaration of Helsinki and reported using the recommendations for reporting randomized clinical trials as defined in the statement of Consolidated Standards of Reporting Randomized Clinical Trials (CONSORT) (Schulz et al., 2010). The study protocol was reviewed and approved by the Ethical Committee of Shiraz University of Medical Sciences (registration number: Shirazums CT-90-5677). The trial protocol was registered in the NIH clinical trials database under registration number: NCT01443702.

All participants returned signed informed consent forms, which are filed at the Department of Phytopharmaceuticals, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

#### 2.2.2. Study design

Participants were recruited from January 2011 to December 2011 in the Shahid Motahari Clinic of the Shiraz University of Medical Sciences according to the approved protocol. All patients understood the purpose and method of the study and agreed to participate with written informed consent. Calcium stones were diagnosed by KUB, ultrasonography, and non-contrast spiral CT scan of the kidney. We also asked patients for a composition analysis of stones they had previously passed (if available). Patients older than 18 years with renal stones 5 mm or bigger in the lower pole of the kidney with or without symptoms such as dysuria, pain in the renal angle or flanks radiating to the groin, or burning micturition were included in the study. Patients with severe urinary tract infection, ureterohydronephrosis, diabetes,

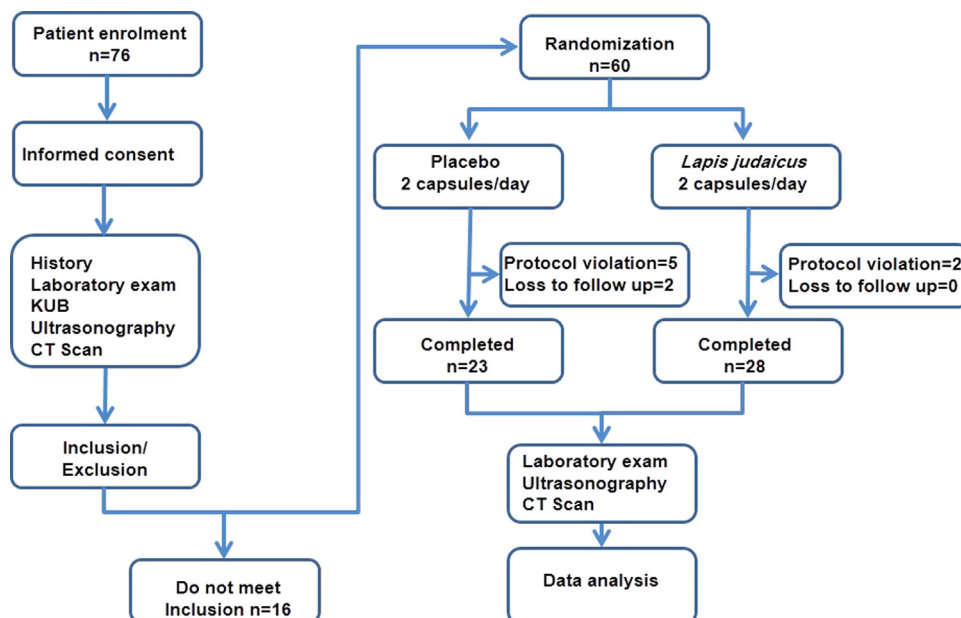


Fig. 1. CONSORT diagram of *Lapis judaicus* safety and kidney stone dissolving efficacy clinical study.

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