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Original Research Article

Marine Plants are the Source of Lead Compounds for Better Alternative Drugs for the Treatment of Kidney Stones

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Abstract

Urinary stones are the one of the oldest and most common affliction in humans. This disease has tormented humans since the earliest records of civilization. Ten percent of men and 3% of women have stone during their adult lives. Genetic, metabolic, environmental and diabetic factors are involved in the pathogenesis of urolithiasis, all of them propitiating the crystallization of salts inside the renal tubules, further retention and growing to form a stone. Moreover, calcium oxalate (CaOx) crystals, the main constituent of human urinary calculi. In this present study, the *in vitro* experiments of marine halophytes on the inhibition of calcium oxalate crystal were tested. Marine halophytes *viz.*, Seagrass (*Syringodium isoetifolium* and *Cymodocea serrulata*) and Seaweeds (*Dictyota dichotoma, Stoechospermum marginatum, Sargassum wightii, Caulerpa scalpelliformis & Valaniopsis pachynema*) were selected for the study. Among the marine halophytes tested, the ethyl alcohol extract of *Caulerpa scalpelliformis* exhibited maximum Calcium oxalate crystals inhibition (83.34±0.015%), which is highly comparable (91.68±0.02) to the standard drug (Positive control - Cystone). So it can be concluded from the present study that, the marine halophytic seaweed extract of *Caulerpa scalpelliformis* can be used as an alternative drug for the treatment of kidney stones.

Keywords

Calcium oxalate inhibition
Caulerpa scalpelliformis
Kidney stones
Marine halophytes
Polaritic solvents
Urolithiasis

Introduction

Herbs are herbal drugs have created interest among the people by its clinically proven effects like immunomodulation, adaptogenic and antimutagenic. Also, the overuse of synthetic drugs, which results in higher incidence of adverse drug reactions, has motivated humans to return to nature for safe remedies (Edwin et al., 2007).

The problem of urinary stones or calculi is a very ancient one and many remedies have been employed

during the ages these stones are found in all parts of the urinary track, the kidney, the ureters and the urinary bladder and may vary considerably in size. Diet containing low amount of inferior quality proteins and high intake of animal proteins might augment the risk of stone formation. The incidence of urolithiasis is very common in northern India compared to southern state. It is speculated that higher incidence may be due to wheat diets. People living in rocks areas, where the climate is hot and dry, seem to be more to urinary calculi disease (Singh et al., 2006). In the present study, an attempt has been made to emphasize on herbal treatment for urinary calculi by using the marine halophytes extracts.

Materials and methods

Collection of marine halophytes

Different species of marine halophytes *viz.,* seaweeds (*Dictyota dichotoma, Stoechospermum marginatum, Sargassum wightii, Caulerpa scalpelliformis & Valaniopsis pachynema*) (Lat.$9^0$17”2.58N; Long. $79^0$9”54.04E) and sea grasses (*Syringodium isoetifolium* and *Cymodocea serrulata*) (Lat.$9^0$44’10”N; Long. $79^0$10’12”E) were collected from southern coast of India and has been authenticated by Dr. K. Eswaran, Scientist, Central Salt and Marine Research Institute, Mandapam , Tamil nadu, India. A voucher specimen have been maintained in the herbarium cabinet facility maintained in the School of Marine Sciences, Alagappa University, Thondi campus sponsored by the Indian Council of Medical Research, New Delhi for reference.

Extraction and processing

Collected samples were air dried and blended with electric mixer and kept for the extraction of bioactive principles. The coarse powder of different plants was used for the extraction. Cold extraction was carried out by using different polaritic solvents (ethyl alcohol, ethyl acetate and diethyl ether) of high polarity by simply soaking the plant samples in the solvents and kept for a week (traditional extraction). After that, the solvents with bioactive compounds were filtered using muslin cloth and kept in the rotary flash evaporator with solvent trap to remove excess solvent residues in the extract.

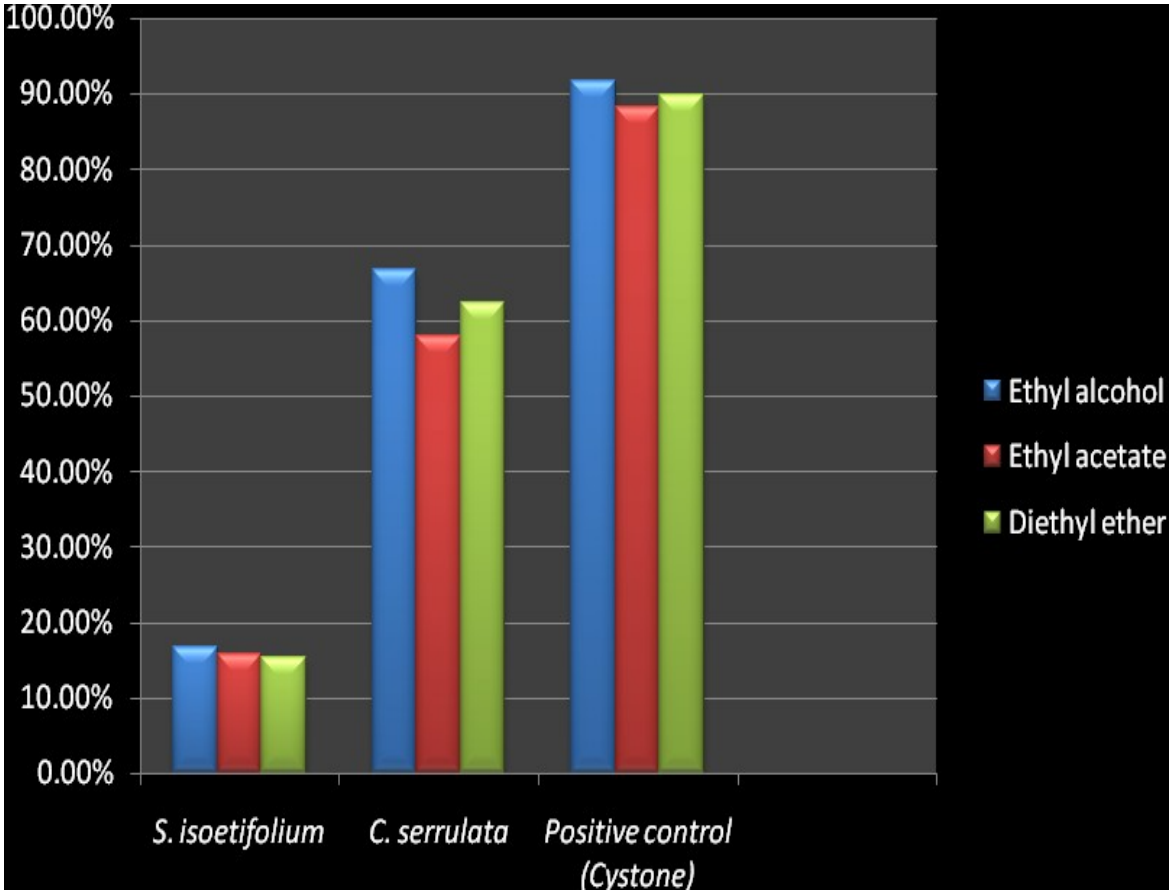
Aqueous extract were prepared with DMSO (Dimethoxy sulphate) and then centrifuged at 1000 rpm so as to obtain the clear supernatant for the study. Five milliliter of 3% calcium chloride was taken and mixed with 5ml of 3% sodium oxalate. When the precipitation occurs, 1% of plant extract was added to that and kept in a shaker for 5 days incubation after that the aqueous phase was filtered for the estimation of free calcium by titration method. Control was maintained without the addition of the test plant extract. Positive control was also maintained with the addition of cystone (standard drug) but without the addition of plant extracts. From both the treated and control samples, 5ml of sample was taken in a conical flask and add with 5 ml of sodium hydroxide followed by a pinch of Murexide indicator. Diluted the solution to 100 ml with distilled water and titrated (take concordant values) against with EDTA until the colour changes from pink to purple. This titre value was taken as A, the standard value of calcium (2mg) was designated as F. The level of free calcium was estimated by using the following formula: Amount of calcium in the sample ($mg.l^{-1}$) = F X A X 1000/sample volume. Factor value of calcium (F) = 2 (mg). The percentage inhibition of calcium oxalate formation= calcium in control – calcium in treatment/calcium in control X 100.

Results and discussion

Urolithiasis is a complex process that results from a succession of several physicochemical events including supersaturation, nucleation, growth, aggregation and retention within the kidneys. Treatment of urolithiasis involves either conventional therapy or interventional procedures. The primary agents in medical management for urolithiasis, has been investigated with calcium channel blockers, steroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and 1-adrenergic receptor antagonists (Hollingsworth et al., 2006). Although calcium channel blockers with or without steroids and/or NSAIDs have shown to be successful in the treatment. Blockers, with their high success rates have become the leading candidate in medical therapy (Lipkin and Shah, 2006). However, these treatment regimens are not free from side effects. The endoscopic stone management has allowed kidney stones to be treated using minimally invasive techniques, which have increased success rates and decreased treatment-related morbidity. These advances include shock wave lithotripsy (SWL), ureteroscopy, and percutaneous nephrostolithotomy. Although these approaches are less invasive than the traditional open surgical approaches, they are expensive and have inherent risks (Segura et al., 1997). Due to the high cost and adverse effects of minimally invasive techniques, and recurrence

alternative treatment modalities with phytotherapeutic agents have become the mainstay of medical therapy. Several terrestrial plants have been tested scientifically (Chaudhary et al., 2010) and traditionally (Miyaoka and Monga, 2009) understood for the treatment of urinary calculi but no attempt has been made with the marine plants. Hence, the present study has been undertaken to findout the bioactive compounds present in the marine halophytic plants for the treatment of urinary calculi. In the present study, standard drug cystone and marine plant extract on the calcium oxalate inhibition was carried out and it reveals that, among the marine halophytic seagrass species the ethyl alcohol extract of *Cymodocea serulata* (66.66±0.005%) showed maximum inhibition of calcium oxalate when compared with the other chosen seagrass species (Fig. 1).

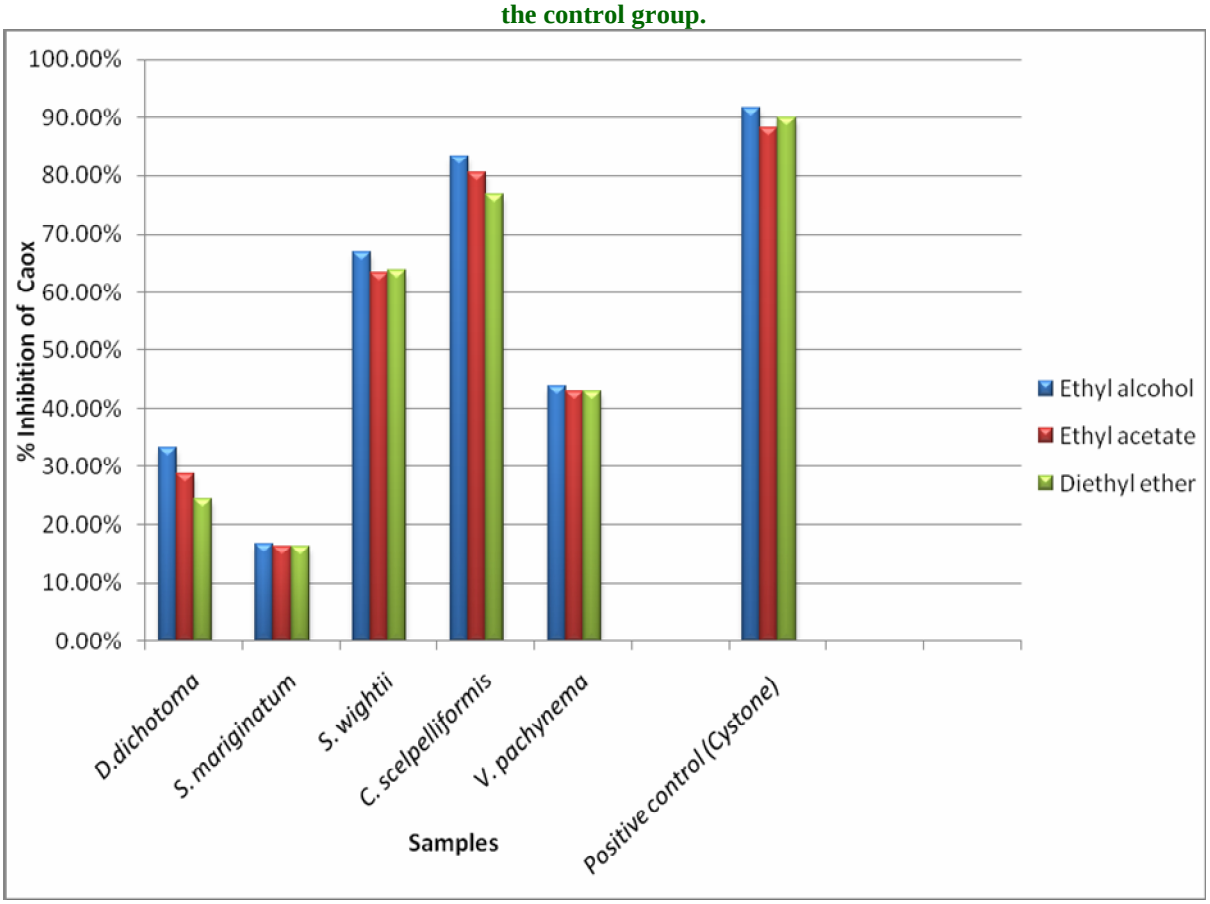
Fig. 1: Percentage inhibition of calcium oxalate formation by different polaritic solvent seagrass extracts compared with the control group.



Moreover, among the chosen seaweed species, ethyl alcohol extract of *Caulerpa scalpelliformis* showed the maximum calcium oxalate inhibition (83.34±0.015%) when compared with the other seaweed marine halophytic species when compared with the control (91.68±0.02%) (Fig. 2). It is already proved that, the marine halophytic plants posses antimicrobial (Ravikumar et al., 2011; Sona et al., 2015), antiplasmodial (Jacob et al., 2012; Margret beula et al., 2015), antifungal (Prabhakar et al., 2008), antiinflammatory and analgesic (Guzman et al., 2001) activities. It has been reported that, the terrestrial plant *Terminalia arjuna* bark was found to inhibits the formation of Calcium oxalate crystals (Chaudhary et al., 2010). Unnati et al. (2013) reported that, the chloroform and benzene extracts of medicinal plants *Dolichos biflorus* Linn and standard drug (cystone) were used for dissolving calcium oxalate kidney stones. Phenolic, flavonoids and steroids compound have been isolated from the plant extract and the aqueous fractions showed highest dissolution of stones. But, when comparing with the standard drug cystone, the phenolic and flavonoids fractions were less effective. But, in the present study the effect of halophytic plant extract of *Caulerpa scalpelliformis* on inhibition of calcium oxalate is highly comparable to the standard drug cystone (Fig. 2).

Similarly Shoaib et al. (2014) reported that, the plants extract of *Clitoria ternatea* tested for *in vitro* calcium oxalate formation and found to inhibit the calcium oxalate precipitation, which is comparable activity to that of cystone in terms of inhibiting the formation of calcium oxalate precipitation. Now, treatment of lithiasis mainly targets the potentiation of the defensive system along with lowering of stone formation. Recent technological advances have renewed interest in natural products in drug discovery.

Fig. 2: Percentage inhibition of calcium oxalate formation by different polaritic solvent seaweed extracts compared with the control group.



Conclusion

Hence it can be concluded that, the marine halophytes selected for this study particularly the different polaritic solvent extracts of *Caulerpa scalpelliformis* has potential compounds to inhibit the formation of calcium oxalate crystals and can be used as an alternate for the treatment of kidney stones. *In vivo* scientific evaluation and the safe and efficacy of the drugs of marine origin for the treatment of kidney stones are in progress.

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