Sir,

This letter is in context to the article published in your journal titled, “Antiurolithiatic effect of lithocare (LC) against ethylene glycol (EG)-induced urolithiasis in Wistar rats.”[1] This was a well-designed interventional study with clearly defined intervention and availability of control and comparator (Cystone). However, there are some limitations which deserve mention.

In terms of methodology, the EG rat model is not without limitations. To decrease crystal formation after EG ingestion, intervention may work at any level in the metabolism of the EG or beyond. The question as to whether the new agent under study decreases crystallization and deposition of calcium oxalate or whether it acts on EG metabolism itself is unanswered. The rate limiting step in EG metabolism catalyzed by alcohol dehydrogenase is the site of action of the conventional antidotes to human EG poisoning; ethanol and 4-methylpyrazole (fomepizole). Both these agents increase the half-life of EG allowing the liver time to metabolize EG and excrete it via the kidneys.[2] Monitoring the serum concentration of EG would have differentiated between drug action affecting the metabolism of EG to oxalic acid as opposed to primarily creating conditions unfavorable for deposition of calcium oxalate crystals in the tubules.

Ethanol increases the fraction of EG excreted unchanged in the urine before toxic metabolites are formed. If any of the herbal ingredients were obtained as an ethanolic extract, this would present a confounder (detail unavailable in materials and methods). Similarly, if the preparation contained the vitamins thiamine or pyridoxine, it could facilitate metabolic detoxification of EG since these allow bypass of the regular EG metabolic pathway toward the formation of less toxic products (α-amino-β-ketoacidic acid and glycine, respectively).[3,4]

Regarding choice of comparator; two out of three constitute herbal ingredients of LC were listed to have diuretic effects. Urine output was significantly higher in rats receiving LC as compared to controls. Diuretic action alone would have been expected to decrease crystal accumulation by virtue of preventing supersaturation and retarding the process of crystallization. This is especially pertinent since the rats were given a free access to drinking water. Indeed, administration of a thiazide diuretic would have also resulted in hypocalciuria, hypoxaluria, decreased serum creatinine, serum urea, and blood urea nitrogen.[5] To examine for this effect, an arm treated with EG and diuretic such as a thiazide might have allowed a more valuable comparison than one with Cystone.

Further research will be required to elucidate the active principles and identify the sites of action. The conclusion that the new agent prevents EG-induced urolithiasis and reduced the growth of urinary stones would not be accurate as the experiment dealt with crystalluria and not lithogenesis per se. This assertion is an extrapolation of previous research showing that calcium oxalate crystals form aggregates in the collecting ducts that act as nidus for stone formation.[6]

On the basis of evidence provided, it would be better to conclude that the new agent reduces EG-induced crystalluria in rats and may prove to render benefit in reducing calcium deposition of calcium oxalate crystals in the tubules.

Antiurolithiatic effect of lithocare against ethylene glycol-induced urolithiasis in Wistar rats

Dr. Anant Dhondopant Patil
Correspondence to:
Anant Dhondopant Patil
Institute of Medical Research and Education Trust, Belapur, Navi Mumbai, Maharashtra, India

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oxalate stone formation in human subjects. There is scope for investigation as a novel therapy for EG poisoning by virtue of decreasing calcium oxalate monohydrate crystalluria in addition to the benefit of evident antioxidant properties.

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Conflicts of Interest
There are no conflicts of interest.

Ranil Johann Boaz, Anuj Deep Dangi, Nirmal Thampi John
Department of Urology, Christian Medical College, Vellore, Tamil Nadu, India

Correspondence to:
Dr. Ranil Johann Boaz,
E-mail: jomcizmo@gmail.com

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