

Probiotics Supplements for the Management of Calcium Oxalate Kidney Stones-Are We Ready for it?

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Editorial

The origin of the word probiotic comes from the Greek word "pro" meaning "promoting" and "biotic" meaning "life". The discovery of probiotics came about in the early 20th century, when Elie Metchnikoff, known as the "Father of Probiotics" had observed that rural dwellers in Bulgaria lived to very old ages despite extreme poverty and harsh climate. In October 2013, the International Scientific Association for Probiotics and Prebiotics (ISAPP) define probiotics as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host".

Crystals of calcium oxalate are the most widely recognized kind of kidney stones. Kidney stones are dense masses that form in the kidney when there are increased levels of calcium, oxalate, cystine, or phosphate and very less liquid. Calcium oxalate stones are triggered by too much oxalate in the urine. Oxalate is considered an unusable end product of mammalian metabolism and urinary oxalate is derived from endogenous metabolic sources, primarily produced by the liver [1]. Almost 80-90% of kidney stone forming individuals form calcium oxalate stones and hyperoxaluria is a main risk factor in this kidney stone diseases.

One possible approach to prevent renal stone recurrence is to decrease the consumption of oxalate rich foods. However, albeit such dietary limitation has been accounted to decrease stone recurrence, its long term effectiveness is uncertain. Therefore, other methods aimed to reduce intestinal oxalate absorption have been sought. Both epithelial barriers of the intestine and kidney mediate oxalate balance. Several investigations acknowledged that intestinal commensal bacteria with oxalate degrading activity have the potential to contribute to oxalate homeostasis. Studies have demonstrated that rehashed use of antibiotics can result in the loss of naturally occurring oxalate-degrading bacteria. With this loss, dietary and endogenous oxalate turns out to be more bioavailable both to the mammalian host and intestinal microbiota.

The oxalate tolerance by the human beings and other mammals are often regularly encouraged by the presence of oxalate-degrading microorganisms in their intestinal microbiota. One of the first oxalate-degrading intestinal microbes to be characterized was *Oxalobacter formigenes* as it requires oxalate as a carbon and energy source. In addition ~18 other probiotics have been screened to degrade oxalate but do not require oxalate for its growth. These include species from the genera *Lactobacillus*, *Bifidobacterium*, *Enterococcus*, and *Eubacterium* among others [2]. *O. formigenes* contains a bunch of oxalate degrading enzymes such as oxalate oxidase, oxalate decarboxylase, oxalyl-CoA decarboxylase, and formyl-CoA transferase, which degrade oxalate into formate and carbon-di-oxide. The study conducted by Anbzhagan et al. developed a recombinant *L.*

plantarum NC8 that constitutively expressed heterologous oxalate decarboxylase and degraded oxalate efficiently under *in vitro* conditions [3].

Studies conducted by both Sidhu et al. and Hatch et al. on experimentally induced hyperoxaluric animals with extraneous supplementation of *O. formigenes* daily for two weeks exhibited a 39-80% reduction in excreted urinary oxalate [4,5]. Likewise, humans supplemented with *O. formigenes* for four weeks exhibited a 22-92% reduction in urinary oxalate content. In addition to *O. formigenes*, a few *lactobacilli* and *bifido-bacteria* represent potential contender for use in the anticipation and treatment of hyperoxaluria. One of the first studies on probiotic supplementation to human brings provided very promising results, where urinary and fecal oxalate levels were reduced in patients with idiopathic hyperoxaluria after treatment with a mixture of three *Lactobacillus* strains (*L. acidophilus*, *L. plantarum* and *L. brevis*), together with *B. infantis* and *Streptococcus thermophilus* [6]. The clinical trial conducted by Lieske et al. at Mayo Clinic, Rochester (US) used two probiotic preparations (Agri-King Synbiotic and Oxadrop) on urinary oxalate excretion in patients with mild hyperoxaluria. Probiotics supplements and placebo were given to patients for 4 weeks and found no change from baseline for any of the groups. The study finally concluded that probiotics did not influenced urinary oxalate levels in patients on a restricted oxalate diet. Rather, this investigation recommends that dietary oxalate limitation is helpful for kidney stone counteractive action [7,8].

Google search indicated several such indigenous probiotics supplements are available in the market for people consumption, without proper validation and analysis. The major drawback concerned with all these products could be the use of freeze dried microbes or granules. *O. formigenes* is a strict anaerobic organism and all other probiotics are facultative and an aerobic organism, co-administrating these microbes as consortia requires numerous investigations. It is imperative to check its cell viability and intestinal colonization, because of low pH of the stomach and the presence of bile salts in the small intestine are the main reasons for the dramatic decline in viability of delivered cells [9-11]. Despite the fact that various advantages and health benefits are related with probiotics or probiotic food items, but also there are few risks that are related with probiotic treatment. Probiotics can interact with commensal microbes and can likewise directly affect the host. Understanding these collaborations is one of the key difficulties for future research.

Nutraceutical market indicated that probiotics are a big and rapidly growing business, with annual global sales of products expected to rise to \$42 billion by 2016. Most probiotics are sold as dietary supplements; this means that the companies that make them don't have to test their products and show that they work or that they are safe, so more research is required to confirm that probiotics are safe and effective

and do not have any side effects on the individuals who are consuming those probiotics. In order to improve the efficacy of probiotics, investigations are moving towards targeted delivery of probiotics to enhance the gastrointestinal stability and intestinal colonization. Dodoo et al. conducted a study on *L. acidophilus* after freeze drying and loaded into capsules for site specific delivery into the colon using the floral coating technology. The results confirmed that encapsulated organisms achieved viabilities of approximately 90% in the gastrointestinal tract and these organisms were adhered to the intestinal wall in the range of 64-76% for the products. The study successfully delivered the probiotics in the upper colon region, which becomes essential for success of probiotics as health supplements [12].

To conclude, the probiotics supplements are now broadly used as nutraceuticals and as health supplements. Accessible probiotics seem to be safe but should be avoided for the patients those are at high risk of septicemia and other clinical complications. Therefore, healthcare regulators and investigators should consider few points such as nutraceuticals should be produced with international regulations, advanced studies need to be conducted for target delivery to avoid unnecessary complications, probiotics should not contain any virulence, side effects, resistance genes or antibiotic resistance genes and should offer characterized health benefits to the individuals.

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