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3.3.2. NUMBER OF BOOKS AND CHAPTERS IN EDITED VOLUMES/BOOKS PUBLISHED AND PAPERS PUBLISHED IN NATIONAL/ INTERNATIONAL CONFERENCE PROCEEDINGS PER TEACHER DURING YEAR

NAMES OF THE AUTHOR

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Therapeutic Applications of Microbial Enzymes in the Management of Kidney Stone Diseases

Shruti Gupta and Shamsher Singh Kanwar

Abstract
Urolithiasis is a terrible pathological condition marked by the presence and formation of kidney stones. It affects around 3–20% of the community in the world. Several environmental, physiological, and nutritional conditions affect this disease. Not only the food sources but also the body's own metabolism and up-oxalate content in the human body. The increased intake of oxalate leads to hyperoxaluria, which often results in the formation of calcium oxalate stones, commonly known as kidney stones. The incidence of kidney stones is very common, and the current therapeutic measure of its cure is not much effective. Therefore, some therapeutic approaches are needed. In the last few years, the use of gut microorganisms with oxalate-degrading activity has emerged as an excellent therapeutic approach to treat kidney stones. As the genes responsible for oxalate-degrading enzymes are not found in humans, use of bacterial enzymes with the ability to degrade oxalate in intestinal digestion has a significant therapeutic impact. This chapter summarizes the roles of microbial enzymes produced by gut microorganisms in the solubilization of the dietary oxalate, and their potential applications in kidney stone diseases.

13.1 Introduction
Kidney stone or urolithiasis is a condition primarily attributed to the deposition of an enhanced level of calcium oxalate in the form of crystals due to supersaturation (of calcium oxalate) during removal of waste from urine (Peck et al. 2016). Although oxalic acid is a general component present in human diet, it is also endogenously

13.2 Role of the Gut Microbiome in Oxalate Degradation
Formation of oxalate stones in humans may be prevented by two symbiotically existing bacterial genera, *Clostridium* and *Lactobacillus*, in the gut. Both bacterial genera have been found to act on some fundamental pathways by the utilization of their oxalate-degrading enzymes (Gault et al. 2017). It has also been hypothesized that the *Clostridium* *thermocellum*, a Gram-negative, obligate anaerobe found in the gastrointestinal tract and in humans, performs a significant role in modulating mammalian oxalate homeostasis (Gupta et al. 2005). The bacterium *C. thermocellum* colonizes the gut in nearly 70–80% of the healthy population and utilizes oxalate as the sole material for energy and carbon source. Formyl-CoA transferase and oxalyl-CoA decarboxylase are the two enzymes from *C. thermocellum*, which catalyze oxalate degradation reaction which results in elevation of oxalate and lactate level (Gutierrez et al. 2010). Further, oxalate is broken down into CO₂ and formate, which is further metabolized and excreted via the liver (Hooper et al. 2005). It has been found that in standard colonization conditions *C. thermocellum* can degrade more than 1 g of oxalate per day. However, attempts to culture this bacterium out of fecal specimens have given low colony counts, less than 10⁶ CFU per gram of wet sample (Alonso and Cook 1993). An investigation by Peck et al. (2016) in most of the cases gut of children between the age of 1 and 6 years is more naturally colonized by *C. thermocellum*, while 20–25% of the colonization is lost during early childhood and colonization in healthy populations (Peck et al. 2016). In addition to *C. thermocellum*, other oxalate-degrading bacterial genera are *Lactobacillus*, *Enterococcus*, *Lactobacillus*, and *Bifidobacterium*. Amongst them, *Enterococcus faecium* uses oxalate as a sole carbon and energy source in a nutrient-deficient environment whereas it can also compete other substrates for growth (Miller and Thuring 2012). In some circumstances, along with other microflora, natural colonization of *C. thermocellum* in the gut is affected. However, continuous use of antibiotics, e.g., in patients with cystic fibrosis, or therapeutic use in diseases such as Crohn's disease also weakens kidney stone formation (Guzon et al. 2004; Hsieh 2014).

13.3 Probiotic Therapies for the Treatment of Kidney Stones
Use of probiotics as a therapeutic and preventive measure in kidney stone and hyperoxaluria has gained much attention. It has been found that in the form of probiotics, aerotolerant *Lactobacillus* and obligate anaerobe *Bifidobacterium* present in the intestine show oxalate-degrading activity, which is considered useful for the prevention of stone formation (Abbas and Foad 2010). Studies confirmed that through treatment with *Bifidobacterium* O138 11141, *Bifidobacterium* topaeus MB 312, and *Bifidobacterium gallicantu* MB 218 strains, the degradation of oxalate could be achieved up to 61%, 52.2%, and 57%, respectively (Guzon et al. 2007). Abbas and

Fig. 13.3 Enzymatic degradation of oxalate

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