

An insight into molecular mechanism of urolithiasis: Identification of proteins from human renal stone matrix as drug targets

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Identification and characterization of kidney stone inhibitors would increase understanding of mechanisms of pathogenesis involved in kidney stone formation (urolithiasis). We have identified novel proteins from human renal stone matrix which can inhibit calcium oxalate (CaOx) crystal nucleation and growth. These proteins were also found to exhibit cytoprotective potential. Out of the five proteins identified, two were anionic proteins (MW ~52, ~41 kDa) with potential inhibitory activity against CaOx crystal nucleation and growth which showed a protective effect on oxalate induced injury on MDCK cells. MALDI-TOF-MS followed by database search on MASCOT server identified these proteins as Programmed cell death protein 4 and Uroporphyrinogen decarboxylase respectively.

In case of humans, programmed cell death protein 4 is up-regulated after initiation of apoptosis and it is well known that oxalate trigger's apoptosis and necrosis in renal cells. Calcium oxalate and oxalate are considered as one of the most harmful endogenous agents which are potential stressors, and capable of inducing injury to confluent tubular epithelial cells. Uroporphyrinogen decarboxylase (URO-D) catalyzes the fifth step in the heme biosynthetic pathway. Subnormal activity of URO-D leads to the most common form of porphyria in humans, porphyria cutanea tarda (PCT). Biochemical findings include accumulation and excretion of large amounts of uroporphyrin and heptacarboxylic porphyrin in the urine which may result in the formation of porphyrin-containing calculi. Proteins which have crystal binding affinity could play a critical role to mediate the earliest events in kidney stone formation. Hence, identification of these proteins not only throws light on the intricate mechanism of kidney stone formation but also provides potential drug targets against urolithiasis.

Biography

Chanderdeep Tandon is a Professor in Biotechnology & Bioinformatics at Jaypee University of Information Technology (JUIT), Waknaghat, Solan, India. He completed his Ph.D. in 1998 from Panjab University, Chandigarh, India and Post-doctoral studies from University of Kansas Medical Center, USA in 2002. He is working in the field of Urolithiasis since last 15 years and has published in the journals of repute. He has published more than 40 papers in journals of repute and is serving as a review board member of various peer-reviewed journals of repute. 5 students have already completed their Ph.D. under his guidance and he is presently guiding 6 Ph.D. students at JUIT, Solan, India. He is a life member of Urological Society of India (USI).

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