

Overview: Biodegradable Metallic Stents for Ureteral Obstruction Treatment

Ureteral stents are commonly employed to restore compromised urological function, with over 1.5 million utilized globally each year. Most commercial ureteral stents are constructed from nondegradable polymeric or metallic materials such as silicone, polyurethane, stainless steel (SS), and nickel (Ni)/titanium (Ti) alloys. Regrettably, more than 80% of patients suffer from stent-associated complications including migration, encrustation, bacterial infection, and fracture, largely attributable to the permanence of these nondegradable implants. Biodegradable stents offer a viable solution to these issues by eliminating the need for secondary procedures to remove stents that are forgotten or nondegradable. Their gradual breakdown also has the potential to reduce surface encrustation, urinary conditioning film formation, and bacterial colonization.

Several biodegradable materials have been explored for ureteral stent use, including polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA). However, their inadequate mechanical properties, high infection rates, and rapid degradation in environments with high urinary pH have curtailed their application. To overcome these limitations, our research team has developed novel zinc-lithium-manganese (Zn-Li-Mn) alloys, which are promising candidates for balloon-expandable stents. These alloys deliver mechanical strengths comparable to titanium, ensuring their machinability and providing the necessary radial strength to maintain an open ureteral lumen. The balloon-expandable stent design, coupled with the biocompatibility of the Zn-Li-Mn alloy, aids in the integration of epithelial tissue within the ureteral lumen and reduces the likelihood of stent migration. Additionally, the biodegradation rate of the Zn-Li-Mn alloy can be adjusted by altering the percentages of electrochemically active Li and Mn. Zinc, an essential element for human health, also imparts unique antibacterial properties that enhance the functionality of the Zn-Li-Mn stents.

Based on these findings, our **hypothesis** posits that Zn-Li-Mn alloys represent a new generation of biodegradable ureteral stents, capable of providing superior mechanical strength, stable biodegradation, minimal stent migration, optimal biocompatibility, and antibacterial efficacy. The **objectives** of this study are to explore the most effective compositions and configurations of the Zn-Li-Mn alloys, fabricate biodegradable metallic ureteral stents, and test their efficacy both in vitro and in vivo, across three related but distinct specific aims:

Aim 1: Optimize and fabricate Zn-Li-Mn ureteral stents with superior mechanical and physical properties. Based on preliminary studies, a series of Zn-Li-Mn alloys with varying Li and Mn percentages will be created by vacuum arc-melting and extrusion, then assessed for their microstructure and mechanical properties using SEM-EDS, XRD, ICP-AES, tensile, and uniaxial compression tests. The goal is to produce alloys with adequate mechanical strength and an elongation-to-failure ratio that ensures durability and flexibility.

Aim 2: Evaluate the biodegradation, biocompatibility, and antibacterial properties of the stents in vitro. The degradation of the Zn-Li-Mn alloy will be tested through immersion and electrochemical corrosion experiments in simulated urine fluids (SUF). Biocompatibility will be assessed by monitoring cell growth and proliferation across urothelial epithelial, endothelial, and smooth muscle cell models. Antibacterial activity against both Gram-positive and Gram-negative bacteria will be determined using the spread plate method and bacterial morphology via SEM imaging.

Aim 3: Investigate the biodegradation, migration, encrustation, tissue responses, and antibacterial performance of the stents in vivo. Zn-Li-Mn alloy balloon-expandable stents will be implanted in diseased minipig models with either ureteral obstruction or urinary tract infection (UTI). The degradation, migration, and encrustation of the stents will be monitored using Micro-CT and SEM imaging, while ultrasonography and ureteroscopy will assess ureteral patency and diameter. Histological and immunohistochemical examinations will evaluate reendothelialization, inflammation, and immune responses. Urination frequency and urinalysis will help determine the overall effectiveness of the stenting, and site infections will be monitored to validate the stents' antibacterial efficacy.