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Dual-layer drug release system based on ureteral stents inhibits the formation of ureteral stricture

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ABSTRACT

Ureteral stricture is a common urological condition caused by the proliferation of scar tissue at the site of the stenosis. Effectively inhibition of scar tissue proliferation at ureter is key to preventing stenosis after ureteral injury. Retention of an anti-fibrotic-loaded ureteral stent tube that gradually releases the drug can inhibit scar tissue proliferation, thus preventing and treating ureteral stricture. In this study, double layers drug release system was used to carry pirfenidone to create ureteral stent tubes for preventing ureteral stricture. Long-term sustained release of pirfenidone was assessed, and the anti-stenosis drug was continuously released by the stent, which also provided drainage support. Drug release data showed that the stent tube experiments rapidly released pirfenidone over the first 5 days, with the release becoming stable and gradual over the subsequent 9 days. *In vitro* data showed that the stent tube had a sustained inhibitory effect on human ureteral smooth muscle cells, a significant inhibitory effect on macrophages and an anti-inflammatory factor release effect. More importantly, *in vivo* data showed that the stent tube had a significant inhibitory effect on ureteral stricture formation in a model of porcine ureteral stricture. These results suggested that the proposed stent tube, a novel pirfenidone sustained-release stent, can effectively inhibit the formation and progression of ureteral stenosis *in vitro* and *in vivo*.

1. Introduction

Ureteral stricture is a common urological condition characterized by a narrower than normal ureteral lumen, resulting in various degrees of upper urinary tract obstruction and hydronephrosis. The causes of ureteral stricture can be categorized as either congenital or acquired. The most common congenital cause is obstruction of the pelvic ureteral junction, and acquired causes are divided into exogenous and endogenous. Exogenous stenosis caused by pelvic tumor compression, retroperitoneal fibrosis, haemangioma, trauma and medically induced injury, whereas endogenous ureteral stricture can caused by stones, ureteral tumors, surgical injury, or radiotherapy [1–3]. Upper urinary tract obstruction due to ureteral stricture can lead to varying degrees of hydronephrosis and impaired renal function, resulting in serious complications that can adversely impact the quality of life of patients and even endanger their lives; it also imposes a huge economic burden on the state, society, and patients' families [4,5].

Current treatments for ureteral stricture has been developed depending on the specifics of the stenotic lesion, such as endoscopic treatment that includes ureteral dilation (ureteroscopic body dilation, balloon dilation, etc.) and endoureterotomy [6–8], laparoscopic or robot-assisted laparoscopic-shaping surgery, intestinal or appendiceal substitution of the ureter, and lingual/buccal mucosa substitution of the ureter [9–12]. Regardless of the treatment modality, a ureteral stent must be left in place after surgery to support the ureter and promote healing and reconstruction, prevent urinary extravasation, avoid

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