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Astragalus mongholicus Bunge and Panax notoginseng formula (A&P) Improves Renal Fibrosis in UUO Mice via Inhibiting the Long Non-coding RNA A330074K22Rik and Downregulating Ferroptosis Signaling

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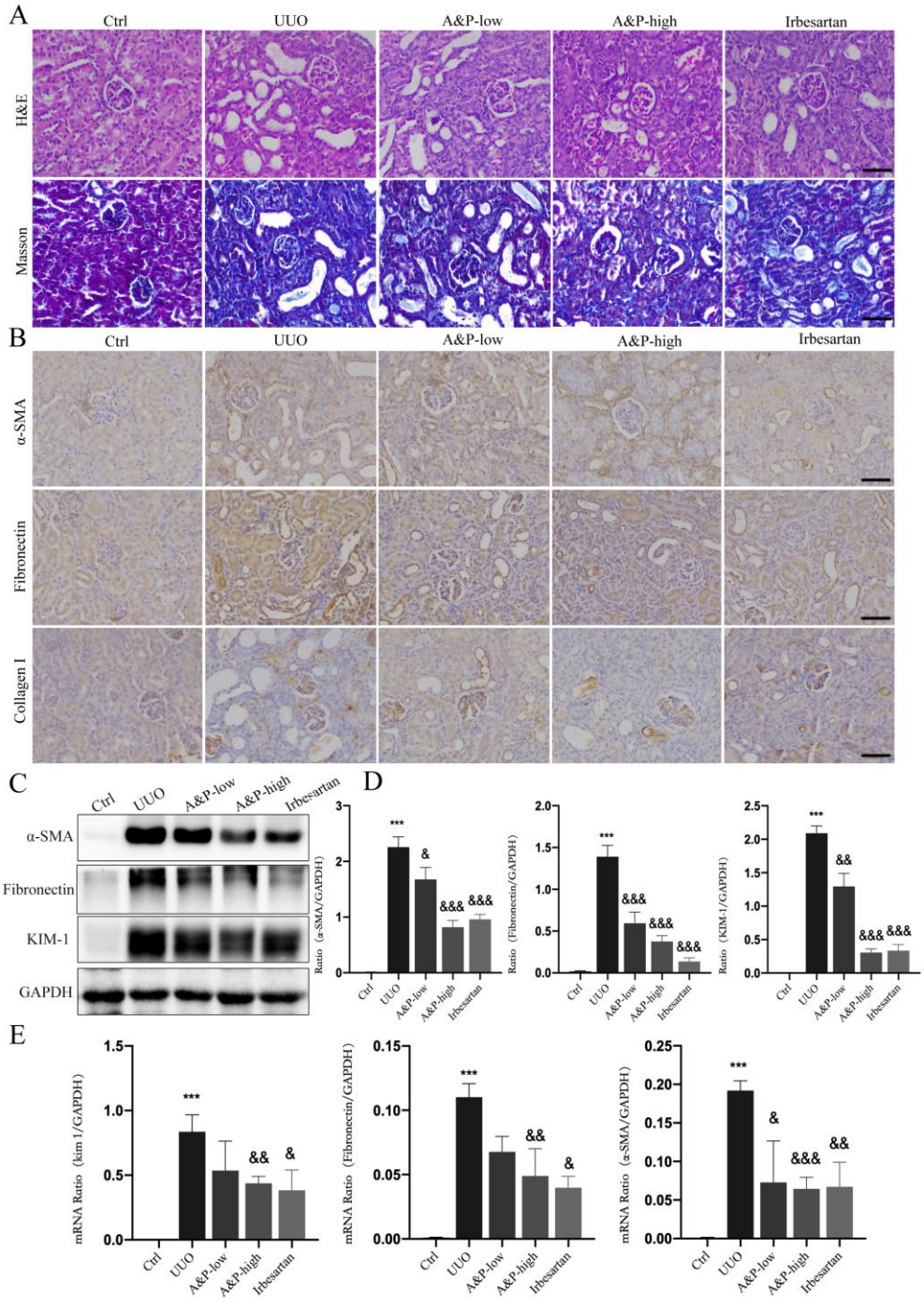
Objectives : Chronic kidney disease (CKD) and its associated end-stage renal disease (ESRD) are significant health problems that pose a threat to human well-being. Renal fibrosis is a common feature and ultimate pathological outcome of various CKD leading to ESRD. The A&P is a refined compound formulated by our research group, which has been clinically administered for over a decade and has demonstrated the ability to improve the inflammatory state of various acute or chronic kidney diseases. However, the underlying mechanism by which A&P ameliorates renal fibrosis remains unclear.
Methods : We established a mouse model by surgically ligating the unilateral ureter to induce renal injury in vivo. And we utilized renal in situ electroporation of a plasmid with low LncRNA A33 expression to establish the unilateral ureteral obstruction（UUO）mouse model. In vitro, we stimulated primary tubular epithelial cells(pTEC) injury using TGF-β1, siRNA-A33, and pcDNA3.1-A33 plasmids were transfected into pTECs to respectively knockdown and overexpress LncRNA A33, and both in vitro and in vivo models were intervened with A&P.
Results : The results demonstrated that A&P effectively alleviated renal fibrosis in mice. Subsequent findings indicated that renal electroporation of a plasmid with reduced LncRNA A33 expression revealed that inhibiting LncRNA A33 significantly improved renal fibrosis in UUO mice. Moreover, A&P effectively suppressed LncRNA A33 expression both in vitro and in vivo. Subsequent downregulation of LncRNA A33 in renal tubular epithelial cells resulted in the downregulation of numerous fibrotic markers, a significant inhibition of LncRNA A33, and a notable reduction in downstream ferroptosis signaling. Cell experiments demonstrated that A&P improved renal fibrosis in UUO mice by inhibiting LncRNA A33 and downregulating ferroptosis signaling.
Conclusions : Through the inhibition of LncRNA A33 and subsequent downregulation of ferroptosis signaling, A&P showed potential as a therapeutic approach for improving renal fibrosis in UUO mice, providing a potential treatment avenue for CKD.

fig1.jpg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Ratio (α-SMA/GAPDH)
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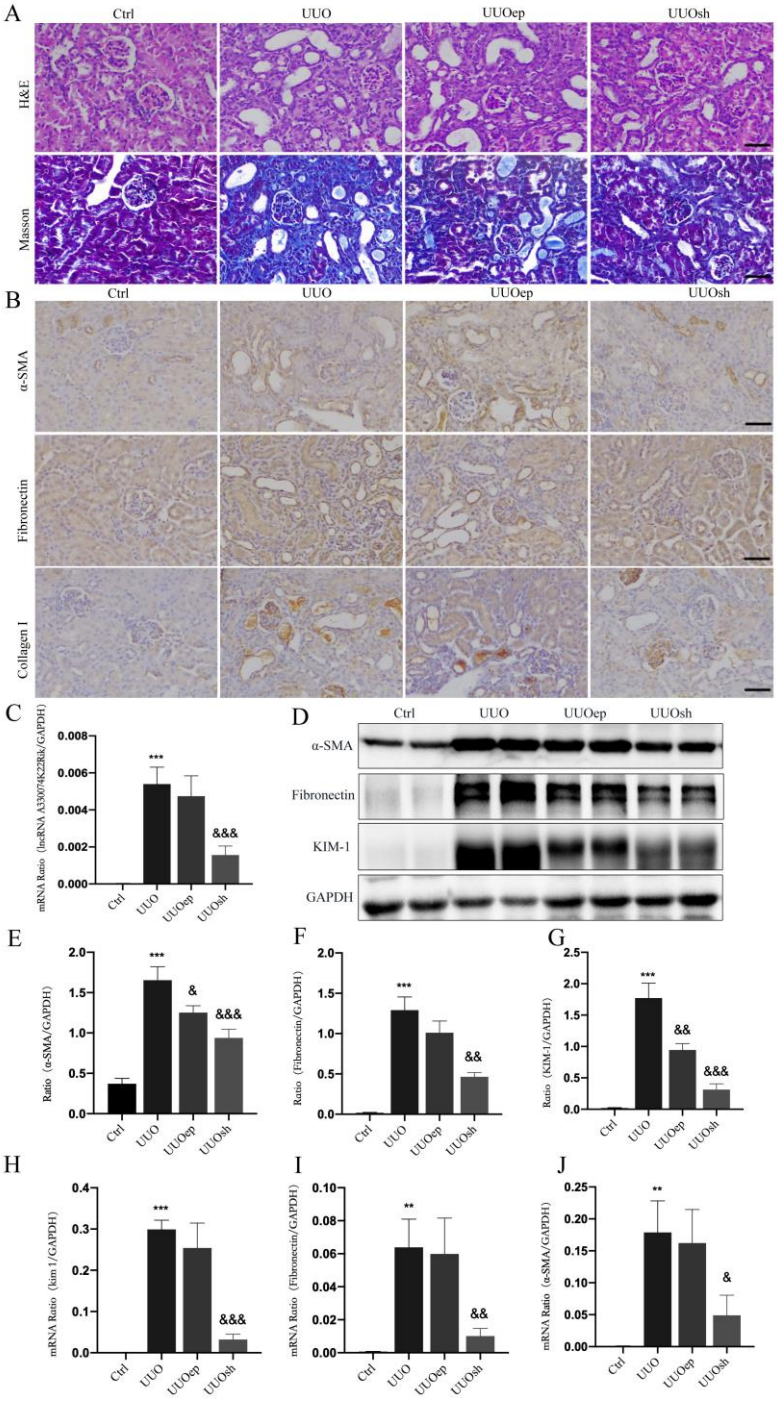
mRNA Ratio (kim 1/GAPDH)
mRNA Ratio (Fibronectin/GAPDH)
mRNA Ratio (α-SMA/GAPDH)

fig1.jpg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Ratio (α-SMA/GAPDH)
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