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## **A water-soluble extract from *Rubus coreanus* can Inhibit Kidney Fibrosis**

**Jeonghwan Lee<sup>1</sup>**, Jin Hyuk Kim<sup>1</sup>, Ara Cho<sup>2</sup>, Jung Pyo Lee<sup>2</sup>

<sup>1</sup>Department of Internal Medicine-Nephrology, SMG-SNU Boramae Medical Center, Korea, Republic of

<sup>2</sup>Department of Internal Medicine-Nephrology, Seoul National University College of Medicine, Korea, Republic of

**Objectives:** *Rubus coreanus* is a wild berry belonging to Rosaceae genus of which application areas have been expanded due to many health effects including anti-oxidation. We aimed to investigate whether treatment with a water-soluble extract of *Rubus coreanus* (MN705) can attenuate kidney fibrosis in unilateral ureteral obstruction (UUO) mice kidney fibrosis and *in vitro* TGF- $\beta$  challenged HK-2 cell models.

**Methods:** Male C57BL/6 mice (7-week-old,  $n = 30$ ) were purchased. Mice were randomly assigned to sham/vehicle group (distilled water,  $n = 6$ ), sham/MN705 (600 mg/kg/day,  $n = 6$ ), UUO/vehicle ( $n = 6$ ), UUO/MN705-low dose (300 mg/kg/day), and UUO/MN705-high dose (600 mg/kg/day) groups. MN705 and distilled water were administered per oral using Zonde needle. After 7 days of pre-treatment, sham or unilateral ureteral obstruction operation performed, and treatment drugs were administered at the same dose for 7 days. In addition, HK-2 cells were cultured and challenged with TGF- $\beta$  (2 ng/ml) with or without extract of *Rubus coreanus* (0.05-0.2 mg/ml).

**Results:** Mice in both groups showed similar body weight and similar serum creatinine levels between groups. In the histopathologic specimen of Masson's trichrome stain, areas of kidney interstitial fibrosis attenuated in the treatment group ( $3.6 \pm 0.9$  % area vs.  $8.7 \pm 3.0$  % area,  $P = 0.03$ ). In the western-blot analysis, protein abundance of collagen-1 (50.6% of control,  $P = 0.04$ ) decreased significantly in the treatment group. *In vitro* experiment, HK-2 cells treated with TGF- $\beta$  and MN705 showed significantly decreased protein expression of fibronectin (64.7% of control in 0.1 mg/ml dose, 22.3% of control in 0.2 mg/ml dose,  $P = 0.01$ ) in a dose-dependent manner.

**Conclusions:** Extract of *Rubus coreanus* attenuates kidney fibrosis in the unilateral ureteral obstruction mice model and TGF- $\beta$ -treated human kidney proximal tubular cells. TGF- $\beta$  related signaling pathway are involved in the development of kidney fibrosis and can be an important treatment target.