JTE-013 supplementation improves erectile dysfunction in rats with streptozotocin-induced type Ⅰ diabetes through inhibition of Rho-kinase pathway and corporal fibrosis

Kang Liu[1,2], Kai Cui[1,2], Rui Li[1,2], Huang Lin[1,2], Tao Wang[1,2], Shaogang Wang[1,2] ,Haihang Feng[3], Jihong Liu[1,2], Bo Wen[3,4], Ke Rao[1,2]

[1]Department of Urology, [2]Institute of Urology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China; [3]Department of Urology, The people's Hospital of Baoan District, Southern Medical University , Shenzhen 518000, Guangdong, China. [4]Department of Urology, The people's Hospital of Shajing District, Guangzhou Medical University , Shenzhen 518104, Guangdong, China.

TONGJI HOSPITAL
TONGJI MEDICAL COLLEGE OF HUST
TONGJI MEDICAL COLLEGE HUAZHONG UNIVERSITY OF SCIENCE & TECHNOLOGY

Introduction and Objective:

Considering ED in patients with diabetes had seriously affected the quality of life. However, these patients showed a poor effect rate for the first-line oral phosphodiesterase type 5 (PDE5) inhibitors. Thus, new treatment methods are urgently needed. To investigate whether JTE-013 supplementation could improve diabetes mellitus-induced erectile dysfunction (DMED).

Method

We used 50 male Sprague-Dawley (SD) rats (8-week-old) for the experiment. Of these, 42 were induced Type Ⅰ DM through the streptozotocin (STZ), and other 8 normal rats constituted the Control group. 8 weeks later, we assessed the erectile function of rats through an apomorphine test. Only rats with DMED were treated with JTE-013 intraperitoneal injection each day for 4 weeks, and other rats were bred in the same condition for 4 weeks. Then erectile function of mice was measured by electrical stimulation of the cavernous nerve and ratio between intracavernosal pressure (ICP) and mean systemic arterial blood pressure (MAP) at the peak of erectile response was calculated. After that penis tissue was harvested. Expression of S1PR2 were measured by immunohistochemistry, immunofluorescence and western blot. And expression of RhoA/ ROCK/p-MYPT1 and ROCK/LIMK2/Cofilin in corpus cavernosum were measured by western blot. The deposition of extracellular collagen was determined by Masson's staining, Apoptosis was detected with TUNEL.

Results

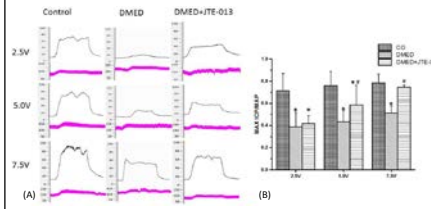

Figure 1. ICP and MAP curves under 2.5V、5.0V、7.5V voltage stimulation and the results of max ICP/MAP
*：P＜0.05 versus Control；#：P＜0.05 versus DMED

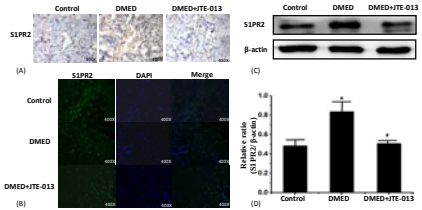

Figure 2. Expressions of S1PR2 in the corpus cavernosum of different groups of rats, *：P＜0.05 versus Control；#：P＜0.05 versus DMED

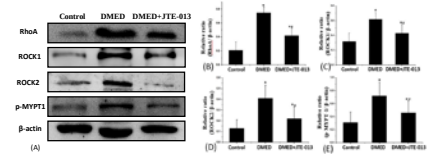

Figure 3. Expressions of RhoA/ ROCK/p-MYPT1 pathways in the corpus cavernosum of different groups of rats, *：P＜0.05 versus Control；#：P＜0.05 versus DMED

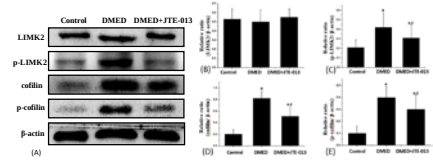

Figure 4. Expressions of ROCK/LIMK2/Cofilin pathways in the corpus cavernosum of different groups of rats, *：P＜0.05 versus Control；#：P＜0.05 versus DMED

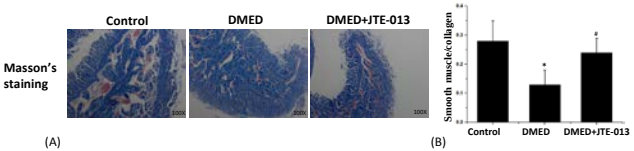

Figure 5. Masson's trichrome staining of different groups of rats, and the ratio of smooth muscle to collagen in the corpus cavernosum of different groups of rats, *：P＜0.05 versus Control；#：P＜0.05 versus DMED

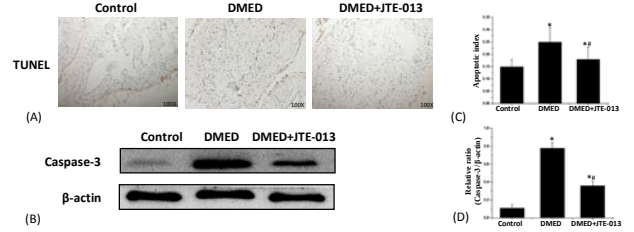

Figure 6. TUNEL of corpus cavernosum in different groups of rats, and the expression of caspase-3 in the corpus cavernosum of different groups of rats, *：P＜0.05 versus Control；#：P＜0.05 versus DMED

Conclusion

JTE-013 supplementation inhibited Rho-kinase pathway and corporal fibrosis, leading ultimately to partial improvement of DMED in rats. Our finding provided evidences for a potential treatment method for DMED.

FOR ORGANIZATION USE ONLY