

**Supplemental Data**

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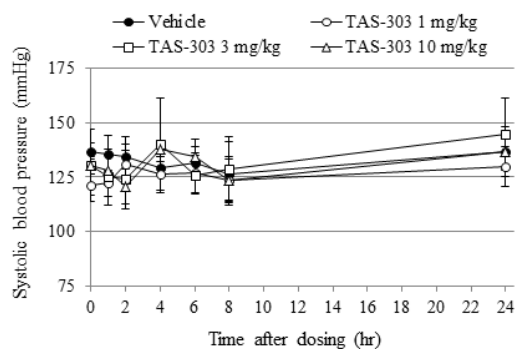
**Title Page**

TAS-303, a novel selective norepinephrine reuptake inhibitor that increases urethral pressure in rats, indicating its potential as a therapeutic agent for stress urinary incontinence

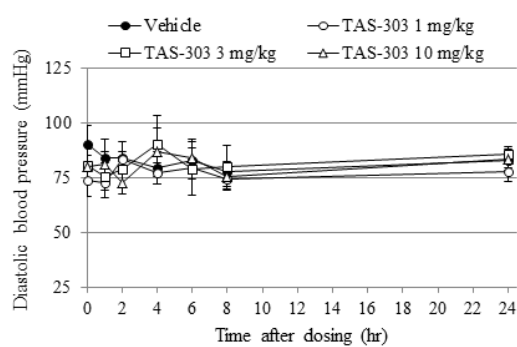
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## Results

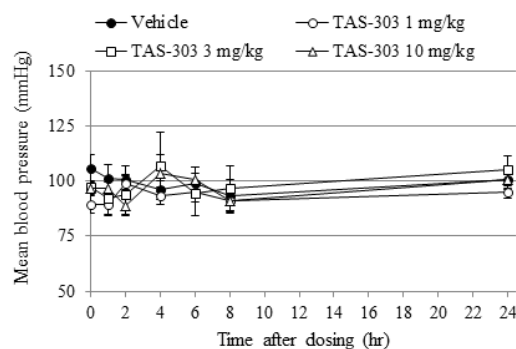
(A) SBP



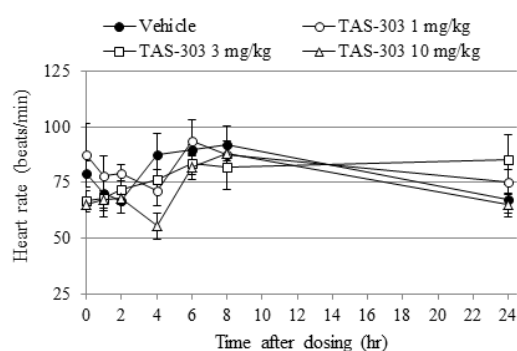
(B) DBP



(C) MBP



(D) HR



Supplemental Figure 1. Effects of TAS-303 on cardiovascular parameters in dogs.

Time course of the effects of a single oral administration of 1, 3, or 10 mg/kg of TAS-303 on systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) was obtained from telemetered dogs under conscious condition. Results are shown as mean  $\pm$  S.E.M. (n = 3).

## **Supplementation Experimental Procedure**

### **Measurements of blood pressure and heart rate in dogs**

Male beagle dogs (8 – 14 kg) implanted with telemetry transmitter were used to investigate the effects of TAS-303 on blood pressure and heart rate. Dogs were housed in stainless steel cages and were offered diet *ad libitum* for at least 6 hours each day. Water was provided *ad libitum*. Environmental controls for the animal room were set to maintain 18 to 26 °C, a relative humidity of 30 to 80%, a minimum of 9 - 12 room air changes/hour, and a 12-hour light/12-hour dark cycle. Before study the animals were habituated to slings, each sling table was equipped with a telemetry-receiving device (Data quest A.R.T., Data-Sciences International), connected via a data-exchange matrix to a PC running the acquisition software (Notocord-hem, Notocord Systems). On the day of study, animals were placed in slings and monitored until cardiovascular parameters stabilized, at which point data were collected for stable 5-consecutive beats to provide baseline data for each animal. At the end of this period either vehicle or TAS-303 (1, 3, or 10 mg/kg) was orally administered via a catheter. Data were collected at 1, 2, 4, 6, 8, 24 hr from the start of the administration. Statistical analysis (repeated two-way ANOVA/Dunnett's test) was performed using SAS version 9.1.3.