

strained and allowed 15 to 30 min in their home cage for their blood pressure and heart rate to stabilize before initiating an experimental protocol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured every 10 min to 3 h after injection from the implanted arterial catheter connected to a Statham P23 pressure transducer (Gould, Oxnard, CA, USA) with display on a Gould RS-3200 physiological recorder (Gould, Cleveland, OH, USA).

Measurement of BP in Anesthetized SHR and Mongrel Dogs

Twenty spontaneous hypertensive rats (SHRs; weight 240 ± 35 g; control group 10; treatment group 10) and 16 mongrel dogs (weight 15 ± 3 kg; control group 8; treatment group 8) were used. Experimental animals used were SHR and Mongrel dogs; SHR, 240 ± 35 g, totally 20 (control group 10, treatment group 10); and Mongrel dogs 15 ± 3 kg, totally 14 (control group 7, treatment group 7). SHRs were anesthetized with 3.5% pentobarbital (Sigma Chemical, St. Louis, MO, USA) administered intraperitoneally at a dosage of 100 mg/kg. Animals were fixed on the table at a constant temperature. The right common carotid artery and external jugular vein of SHRs were cannulated. The external jugular vein was used for intravenous stevioside administration. SBP and DBP were measured through the arterial catheter connected to a Statham P23 pressure transducer (Gould, Oxnard, CA, USA) with the display on a Gould RS-3200 physiological recorder. Mongrel dogs were anesthetized with 3% pentobarbital (Sigma) 1 ml/kg intravenously. The right femoral artery and vein were cannulated for BP measurement and drug administration, respectively. After surgery, animals were allowed to stabilize for 10 min. Treatment group animals were administered different doses of stevioside which was dissolved in pure 0.9% normal saline. Control group animals were given 0.9% normal saline.

Statistics

Data are expressed as the mean \pm SD. Statistical significance was evaluated using the Kruskal-Wallis test when multiple groups were compared; where only intergroup were compared, Student's *t*-test was used.

Repeated measurement of ANOVA was used for intragroup analysis. The level of significance was considered to be $p < 0.05$.

RESULTS

Hypotensive Effect of Stevioside on Conscious SHRs

Stevioside at the dose of 50 mg/kg effectively lowered the SBP and DBP of conscious SHRs. Five minutes after intravenous administration of stevioside, the maximal hypotensive effect on SBP and DBP was $10.8\% \pm 1.7\%$ and $7.8\% \pm 1.2\%$ lower ($p < 0.01$), respectively, when compared with the control (Fig. 2).

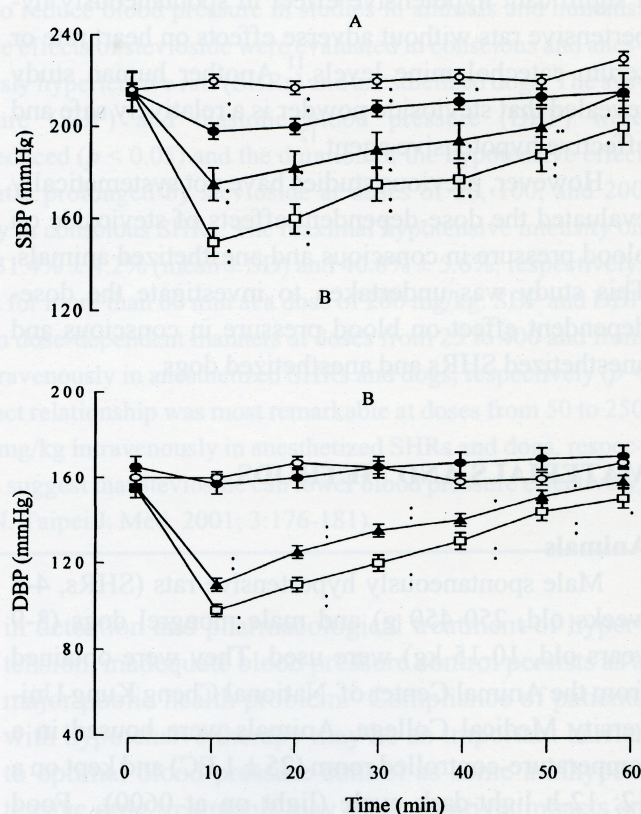


Fig. 2. Effects of intravenous stevioside on systolic blood pressure (A: SBP) and diastolic blood pressure (B: DBP) in conscious spontaneously hypertensive rats. (○) Normal saline 1 ml/kg; (●), (◼), (◻) stevioside at 50, 100, and 200 mg/kg; mean \pm SD, $n = 10$. * $p < 0.05$, ** $p < 0.01$, compared with the control.