PB-51

Hesperidin in Fermented Mikan Tea Induces Anti-hypertensive Effect in SHRs via the Activation of Aortic MasR Axis

Guanzhen GAO[1], Chizumi ABE[1], Alexia M. NECTOUX[1], Shu-Wei HUANG[1], Yuji MIYATA[2], Kazunari TANAKA[3], Takashi TANAKA[4], Haruo YAMAMURA[5] and Toshiro MATSUI[1]*

([1]Faculty of Agriculture, Kyushu University, [2]Nagasaki Agricultural and Forestry Technical Development Center, [3]University of Nagasaki, [4]Graduate School of Biochemical Science, Nagasaki University, [5]Charle Corporation, Ltd.)

Objectives: In previous study, we reported anti-hypertensive effect of a fermented Mikan tea containing hesperidin in mild hypertensive human study[1)], while the underlying mechanism remains unclear. Thus, in this study, the anti-hypertensive mechanism caused by the intake of Mikan tea was investigated using spontaneously hypertensive rats (SHRs).

Methods: Long-term (20 weeks) administration study of hesperidin (50 mg/kg/day) and Mikan tea (50 mg/kg/day) was performed in 8-week-old SHRs. Systolic blood pressure (SBP) and heart rate were measured biweekly. Vasomotor (relaxation/contraction) responses of the aorta taken after the protocol were examined. Levels of Vasomotor-related parameters (Ang II, Ang (1-7), NOx, cAMP) were measured in blood or aorta. Protein expression of AT_1R, AT_2R, and MasR in the aorta was evaluated by a Wes analysis.

Results: Daily intake of hesperidin or Mikan tea to SHRs resulted in a significant SBP reduction of approximately 60 mmHg. Vascular tension experiments revealed that the aorta in hesperidin and Mikan groups maintained potent contraction/vasorelaxation responses by 1 mM phenylephrine/100 μM acetylcholine stimulation, compared to control aorta. The aorta and blood taken from 28-wk SHRs also revealed that pressor Ang II and AT_1R, and depressor Ang (1-7), AT_2R, and NO levels were not influenced by hesperidin or Mikan tea intake, while MasR in the aorta was upregulated in hesperidin group. Along with an increasing aortic cAMP level in the group, it was speculated that the anti-hypertensive effect of hesperidin or Mikan tea was closely associated with the activation of vasorelaxation signaling via the MasR/cAMP axis.

1) Tanaka, K. et al. (2020). *Japanese Pharmacol. Ther.* **48**, 225–235.