Two flavonoid metabolites, 3,4-dihydroxyphenylacetic acid and 4-methylcatechol, relax arteries ex vivo and decrease blood pressure in vivo

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**Fig. S1.** Simplified scheme showing precursors of the phenolic compounds tested in this study. Aglycones, for which the same metabolites were documented (exactly for daidzein, epicatechin, naringenin, quercetin, apigenin), are not shown in the figure. The data in the figure were from the following articles: [1-7]. 3-(2,4-dihydroxyphenyl)propionic acid and 3-hydroxy-4-methoxyphenylacetic acid are not shown, since their metabolic pathways are not yet elucidated.
**Fig. S2.** Vasorelaxant effect of known metabolites of flavonoids on rat aorta. Each curve is the average of at least 3 aortic rings. Data are presented as means ± SEM. The concentration of DMSO is shown below the x axis.
Fig. S3. Change in systolic and diastolic arterial blood pressures after i.v. bolus of DHPA (n = 4) (A) and 4-methylcatechol (n = 7) (B) in SHR rats. Data are shown as means ± SD. For systolic blood pressure: * p < 0.05, ** p < 0.01, *** p < 0.001 and for diastolic blood pressure: + p < 0.05, +++ p < 0.001 vs. saline (dose 0).
Fig. S4. Comparison of dose dependent decrease of systolic (A), diastolic (B) and mean (C) blood pressure after DHPA (n = 4), 4-methylcatechol (n = 7) on SHR. Data on 3HPPA (n = 5), published in Najmanová et al. 2016 [8], are shown for comparison. Data are expressed as means ± SD. Significant difference between DHPA vs. 3HPPA: * p < 0.05, ** p < 0.01, *** p < 0.001; of 4-methylcatechol vs. 3HPPA: *** p < 0.001 and of 4-methylcatechol vs. DHPA: + p < 0.05, ++ p < 0.01, +++ p < 0.001.
**Fig. S5.** Comparison of the effect of DHPA (n = 4) and 4-methylcatechol (n = 7) on heart rate in SHR rats. Data are shown as means ± SD. There were no significant differences vs. the saline (dose 0) or between treatments.
Fig. S6. Change of systolic and diastolic arterial blood pressures during 5 minutes infusion of DHPA (n = 4) (A, C) and 4-methylcatechol (n = 5) (B, D) in SHR rats. Data are shown as means ± SD. p < 0.05 means significant difference of 5 mg/kg/50μl/min vs. saline.
Fig. S7. Dose dependent maximal decrease in systolic (A) and diastolic (B) blood pressure during infusion of DHPA (n = 4) and 4-methylcatechol (n = 5). Data are shown as means ± SD. Data with 3HPPA (not shown) were published in Najmanová et al., 2016 [8].
Fig. S8. Change in stroke volume (A, B), cardiac contractility (C, D) and relaxation (E, F) after DHPA (n = 3) (A, C, E) and 4-methylcatechol (n = 3) (B, D, F). Data are shown as means ± SD. ** p < 0.05 vs. saline (dose 0).
**Fig. S9.** Effect of DHPA (n = 4) (A, C, E) and 4-methylcatechol (n = 3) (B, D, F) on systolic (A, B) and diastolic (C, D) blood pressure and heart rate (E, F) in Wistar:Han rats repeatedly challenged with NE (500 ng.kg$^{-1}$). Results are expressed as means ± SD. * p < 0.05 vs. control group (n = 3). With the exception of 4-methylcatechol in the dose of 0.2 mg.kg$^{-1}$ there were no significant differences between saline and treated group at any dose.
Fig. S10. Modulation of the effects of DHPA (A) and 4-methylcatechol (B) in rat aortic rings pre-contracted with norepinephrine by different inhibitors. A: without any inhibitor (n = 5 rings), + indomethacin (6), + TRAM-34 (6), + TRAM-34 + UCL-1684 (5) and the solvent (6), B: without any inhibitor (n = 5 rings), + indomethacin (6), + TRAM-34 (4), + TRAM-34 + UCL-1684 (4) and the solvent (7). Data are expressed as means ± SEM. The concentration of DMSO is shown below the x axis.
References