Supplementary material

Different mechanisms involved in glucagon-like peptide-1 and liraglutide vasodilatation in rat mesenteric small arteries, Bangshaab and colleagues

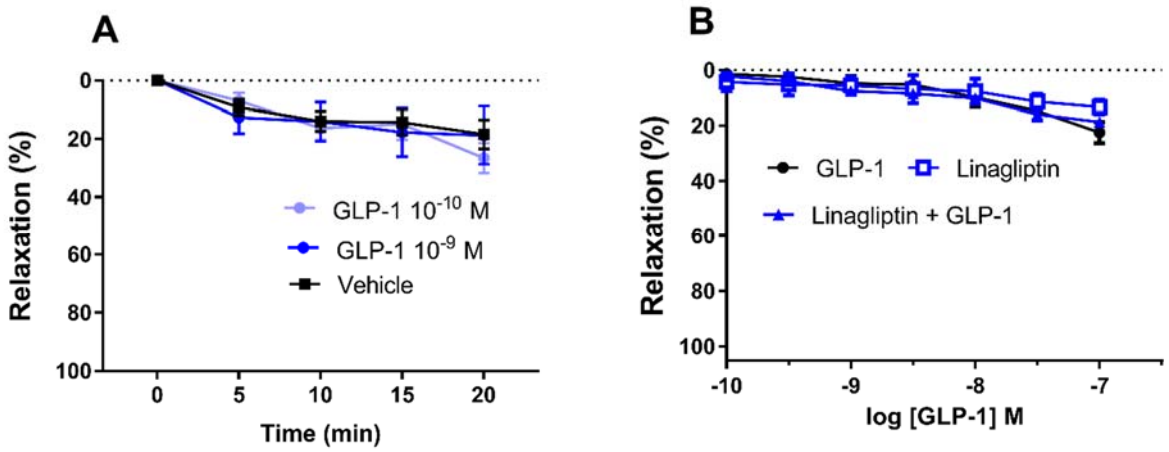

Figure S1: Average effect of single concentrations of GLP-1 (0.1-1 nM) on phenylephrine contracted vessels and the effect of GLP-1 (10^{-8} M) in the absence and the presence of linagliptin (10^{-6} M) in rat mesenteric arteries. (A) Effect of vehicle (n=8) and single concentrations of GLP-1 (n=8) in phenylephrine-contracted arteries. (B) Average data of cumulative concentration-response curves for GLP-1 in the absence (n=6) and the presence (n=7) of the dipeptidyl peptidase 4 (DPP-4) inhibitor linagliptin (10^{-6} M). A time control response was also obtained where vehicle was added in the presence (n=7) of linagliptin (10^{-6} M). Data are presented as means ± s.e.mean. No significant difference between treatments was found.

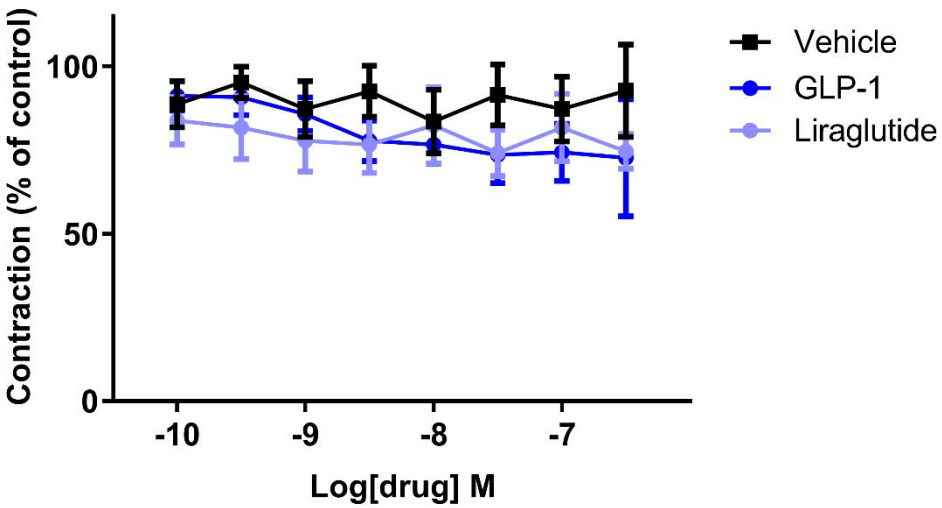

Figure S2: Lack of effect of native GLP-1 and liraglutide on maximum peak of neurogenic contractions in rat mesenteric arteries. Average of traces showing the effect of native GLP-1 and liraglutide on the maximal peak contraction induced by electrical field stimulation, vehicle (n=6), GLP-1 (n=6) and liraglutide (n=5). Peak contractions are presented as percentage of an initial control stimulation. Data are presented as means ± s.e.mean. No significant difference between treatments was found.

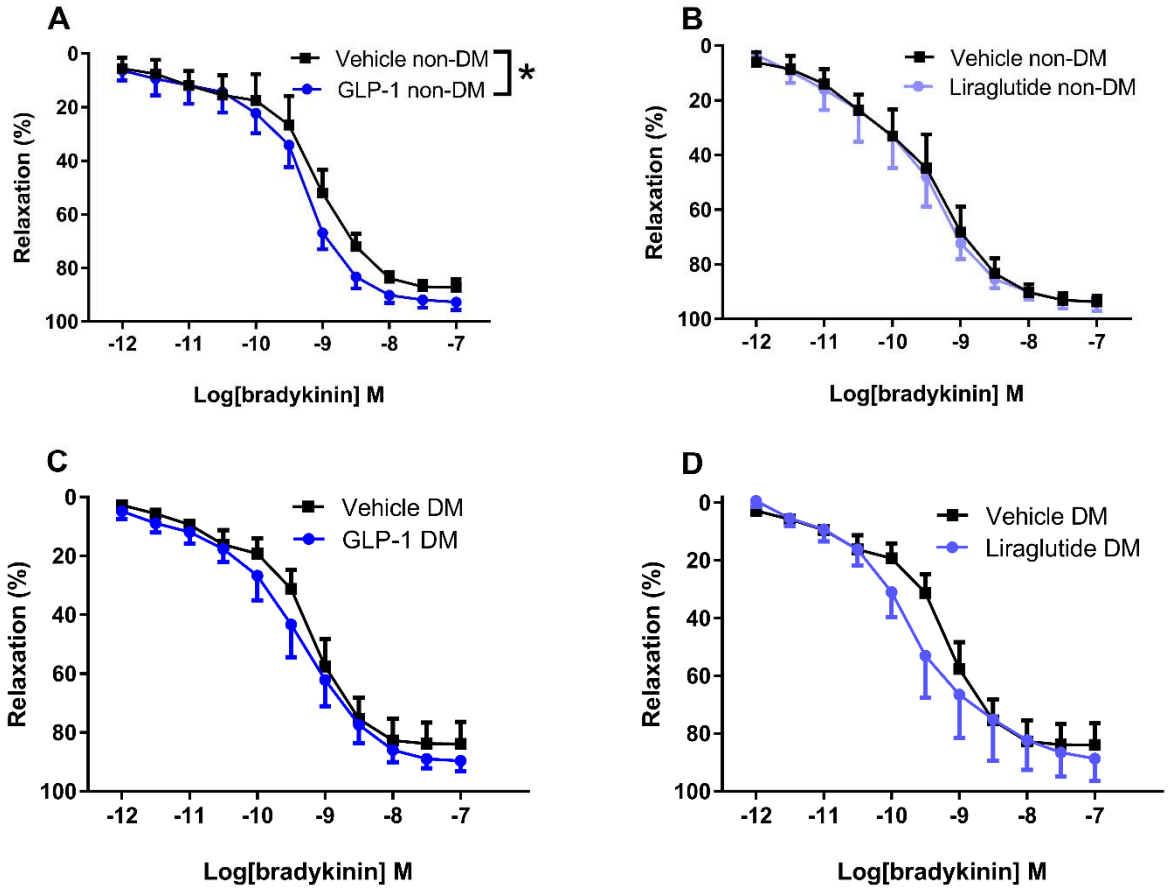

Figure S3: Bradykinin induced relaxation in human subcutaneous arteries from patients without (non-DM) and with diabetes mellitus (DM). (A) Average concentration-response curves for bradykinin in the absence (n=6) and in the presence of GLP-1 (10^{-8} M, n=6), and (B) Concentration-response curves for bradykinin in the absence (n=6) and in the presence of liraglutide (10^{-8} M, n=6) from non-diabetic patients. (C) Average concentration-response curves for bradykinin in the absence (n=4) and in the presence of GLP-1 (10^{-8} M, n=6), and (D) Concentration-response curves for bradykinin in the absence (n=4) and in the presence of liraglutide (10^{-8} M, n=4) from diabetic patients. *P<0.05, 2-way ANOVA followed by Bonferroni post-test

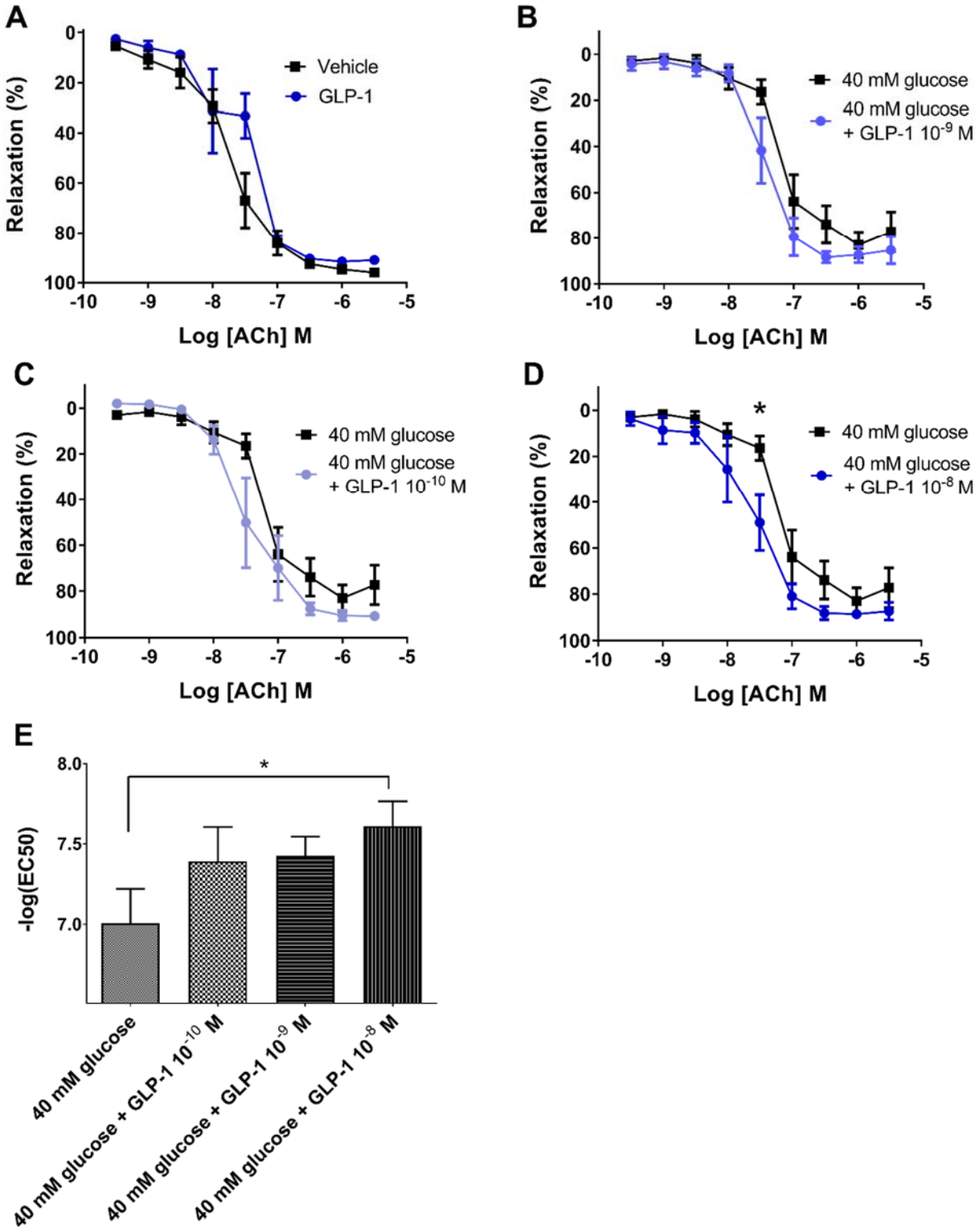

Figure S4: Average effect of single concentrations of GLP-1 (0.1-10 nM) on acetylcholine relaxation in arteries kept in physiological saline solution with high glucose (40 mM). (A)

Acetylcholine concentration-response curves in rat mesenteric arteries kept in 5 mM glucose in the absence (n=4) and the presence of GLP-1 (n=4). (B-D) Acetylcholine concentration-response curves in mesenteric arteries kept at 40 mM glucose in the absence (n=7) and the presence of (B) 0.1 nM (n=5), (C) 1 nM (n=6), and (D) 10 nM (n=6) GLP-1. (E) Concentrations of acetylcholine causing half maximal relaxation presented as $-\log(EC_{50})$ values in mesenteric arteries kept at 40 mM glucose in the absence and the presence of three different concentrations of GLP-1. The results are means±s.e.mean. *P<0.05, 2-way ANOVA followed by Bonferroni post-test. In (E) compared with one-ANOVA followed by t-test.

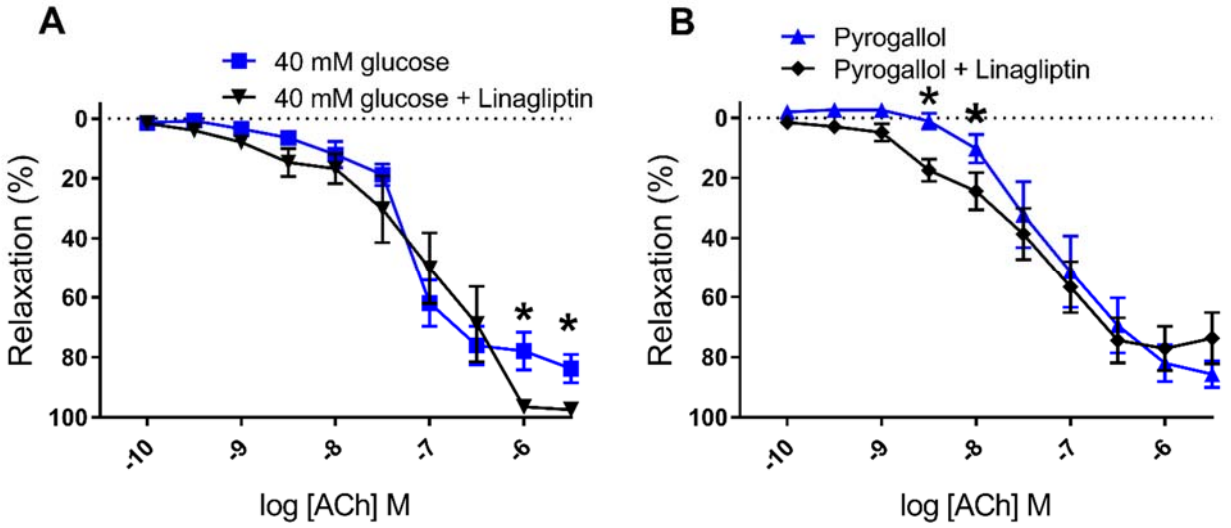

Figure S5: Average effect of single concentrations of linagliptin on acetylcholine relaxation in phenylephrine-contracted vessels exposed to either (A) high glucose or (B) the superoxide generator, pyrogallol. (A) Arteries kept in physiological saline solution with high glucose (40 mM) without (n=8) and with linagliptin (1 µM, n=7). (B) Arteries exposed to pyrogallol (30 µM) in the absence (n=10) and the presence of linagliptin (1 µM, n=10). *P<0.05, 2-way ANOVA followed by Bonferroni post-test.