

Supporting Information

Melanoxetin: A Hydroxylated Flavonoid Attenuates Oxidative Stress and Modulates Insulin Resistance and Glycation Pathways in an Animal Model of Type 2 Diabetes Mellitus

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Table S1: Table detailing antibody names, dilutions, and respective purchase sources for Western Blot analyses.

Primary antibody	Secondary antibody	Dilution	Company
Anti- β -Actin	Mouse	1:1000	Merck
Anti-AMPK total	Rabbit	1:1000	Cell Signalling
Anti-AMPKp	Rabbit	1:1000	Cell Signalling
Anti-Argpyrimidine	Mouse	1:500	Nordic
Anti-Calnexin	Goat	1:1000	Sicgen
Anti-Catalase	Rabbit	1:1000	Abcam
Anti-FBPase	Rabbit	1:1000	Cell Signalling
Anti-GADPH	Goat	1:1000	Sicgen
Anti-GLO1	Rabbit	1:1000	Abcam
Anti-GLUT2	Mouse	1:1000	Abcam
Anti-GLUT4	Mouse	1:1000	Abcam
Anti-Hemeoxygenase	Mouse	1:1000	Abcam
Anti-IR total	Rabbit	1:1000	Santa Cruz
Anti-MG-H1	Mouse	1:500	HylcutBiotech
Anti-Nitrotyrosine	Mouse	1:500	Abcam
Anti-Nrf2	Mouse	1:1000	Santa Cruz
Anti-PPAR α	Rabbit	1:1000	Abcam
Anti-PPAR γ	Rabbit	1:1000	Cell Signalling
Anti-PTP1B	Rabbit	1:1000	Abcam
Anti-SOD1	Rabbit	1:1000	Abcam

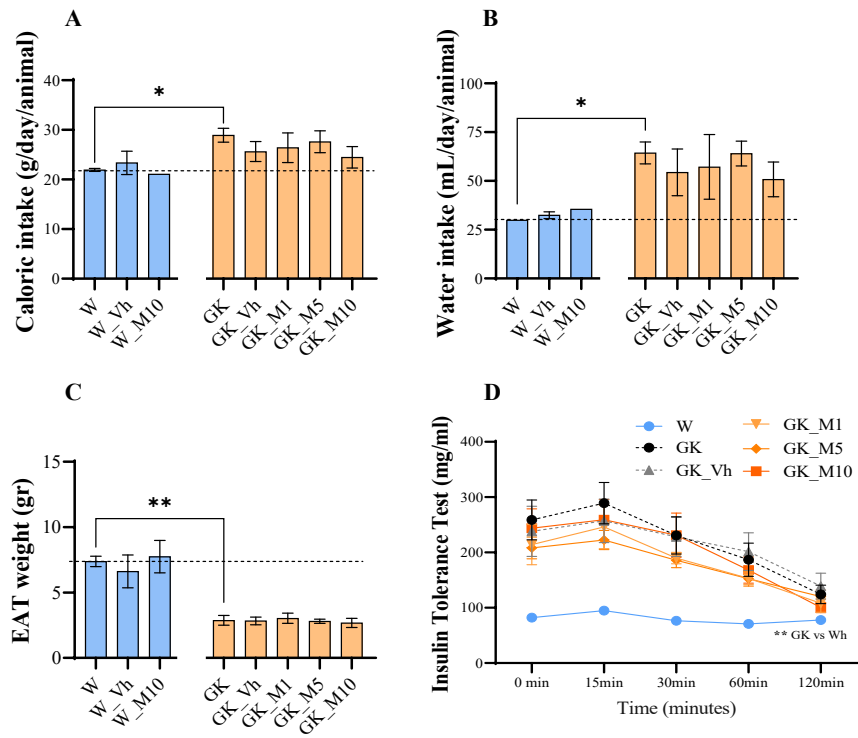


Figure S1: Effect of melanoxetin on caloric intake (A), water intake (B) EAT weight (C) and insulin tolerance test (D) in normal and diabetic animals. Results are expressed as mean \pm SEM of 3 to 6 animals per group. * p <0.05, ** p <0.01.

Epididymal Adipose Tissue

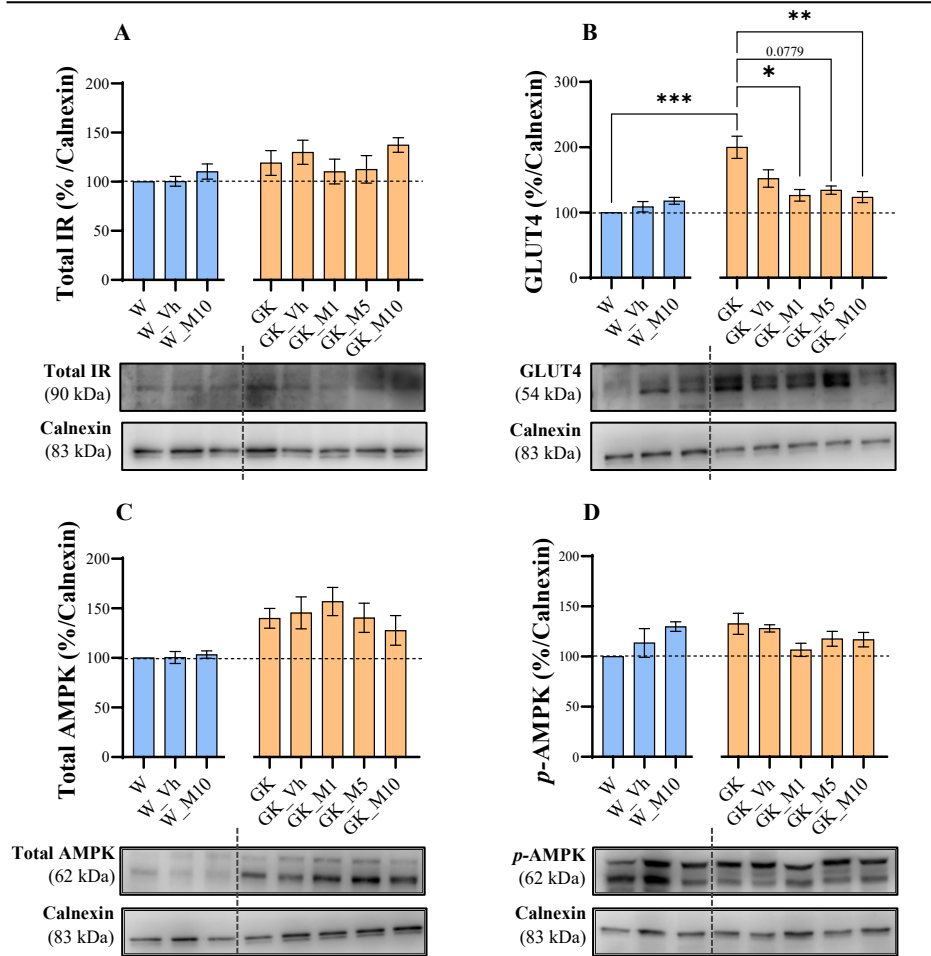


Figure S2: Effect of melanoxetin on the expression of total IR (A), GLUT4 (B), total AMPK (C), and p-AMPK (D) in epididymal adipose tissue. Results are expressed as mean \pm SEM of 3 to 6 animals per group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

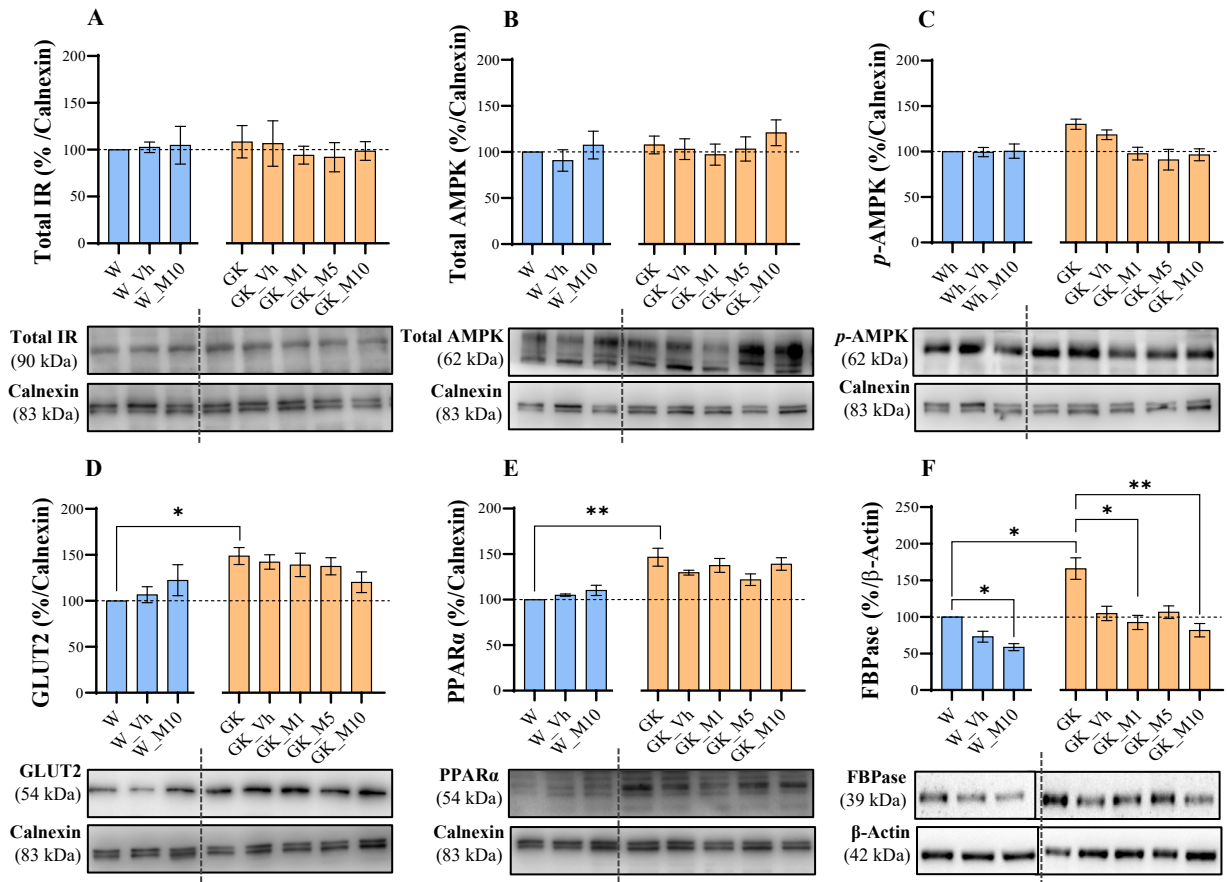


Figure S3: Effect of melanoxinet on the expression of Total IR (A), Total AMPK (B), p-AMPK (C), GLUT2 (D), PPARα (E) and FBPAse (F) in liver tissue. Results are expressed as mean \pm SEM of 3 to 6 animals per group. * p <0.05, ** p <0.01.

Epididymal Adipose Tissue

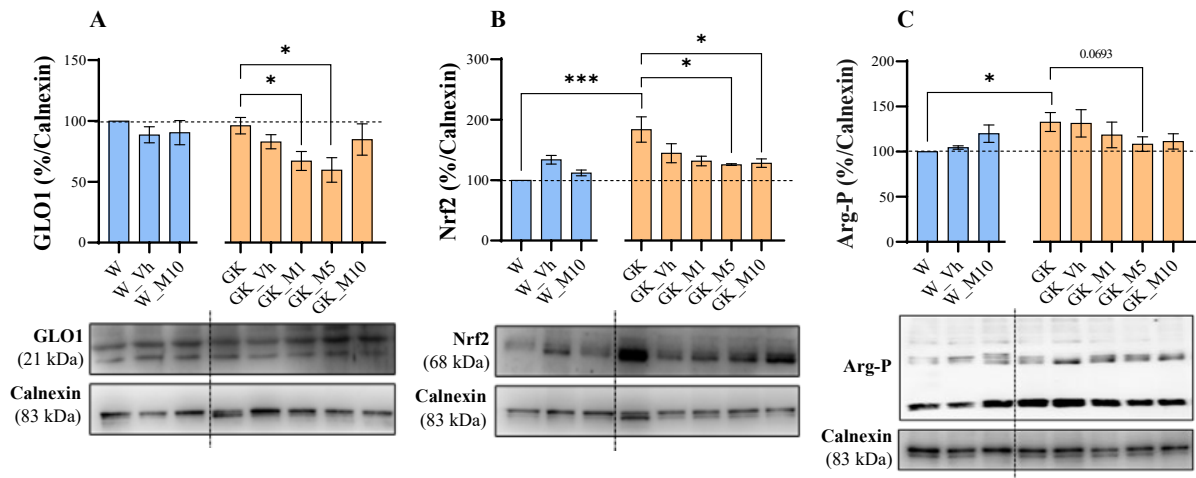


Figure S4: Effect of melanoxinet on the expression of GLO1 (A), Nrf2 (B) and Arg-P (C) in epididymal adipose tissue. Results are expressed as mean \pm SEM of 3 to 6 animals per group. * p <0.05, *** p <0.001.

Liver

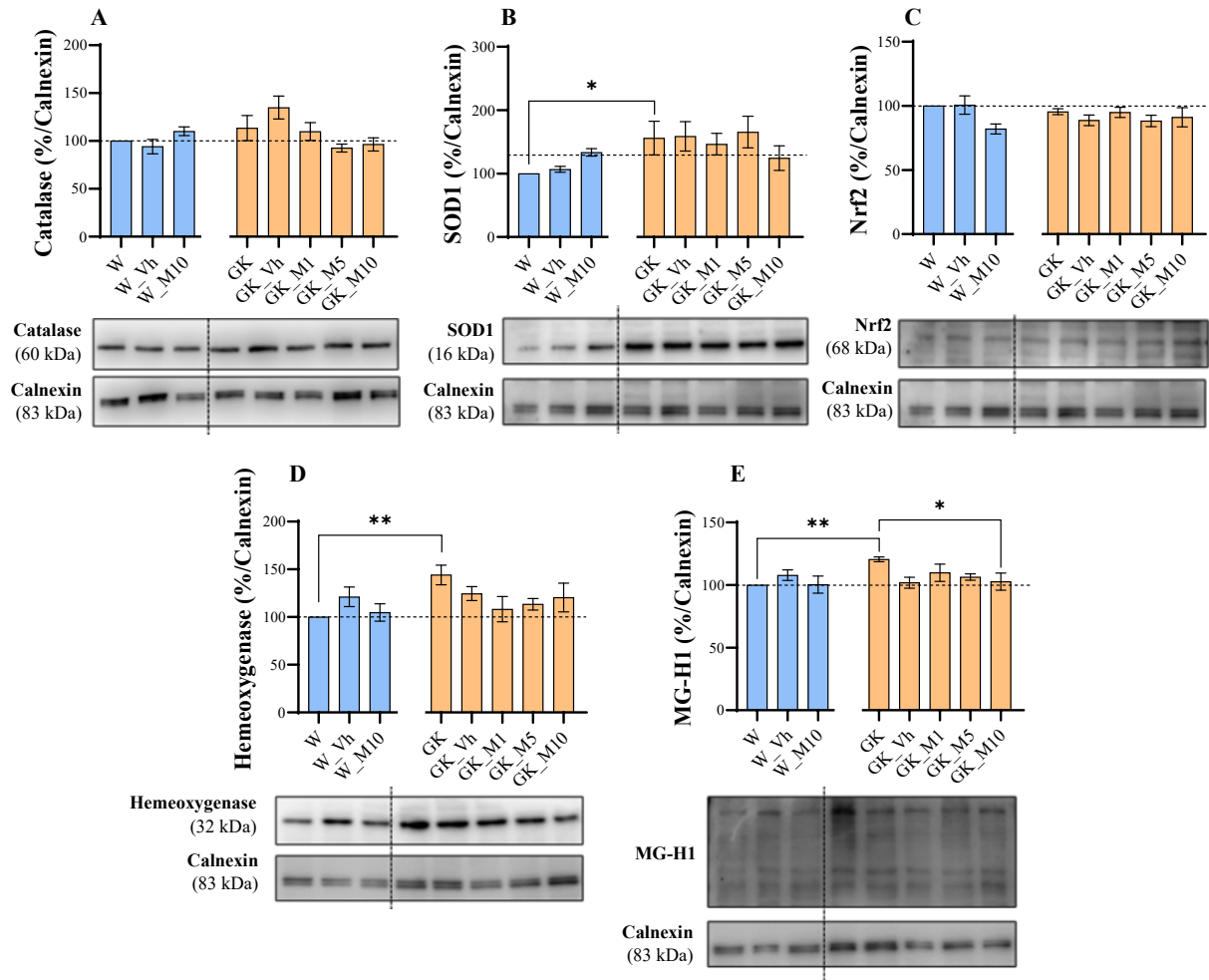


Figure S5: Effect of melanoxetin on the expression of catalase (A), SOD1 (B), Nrf2 (C), hemeoxygenase (D), and MG-H1 (E) in liver tissue. Results are expressed as mean \pm SEM of 3 to 6 animals per group. * $p<0.05$, ** $p<0.01$.

Heart

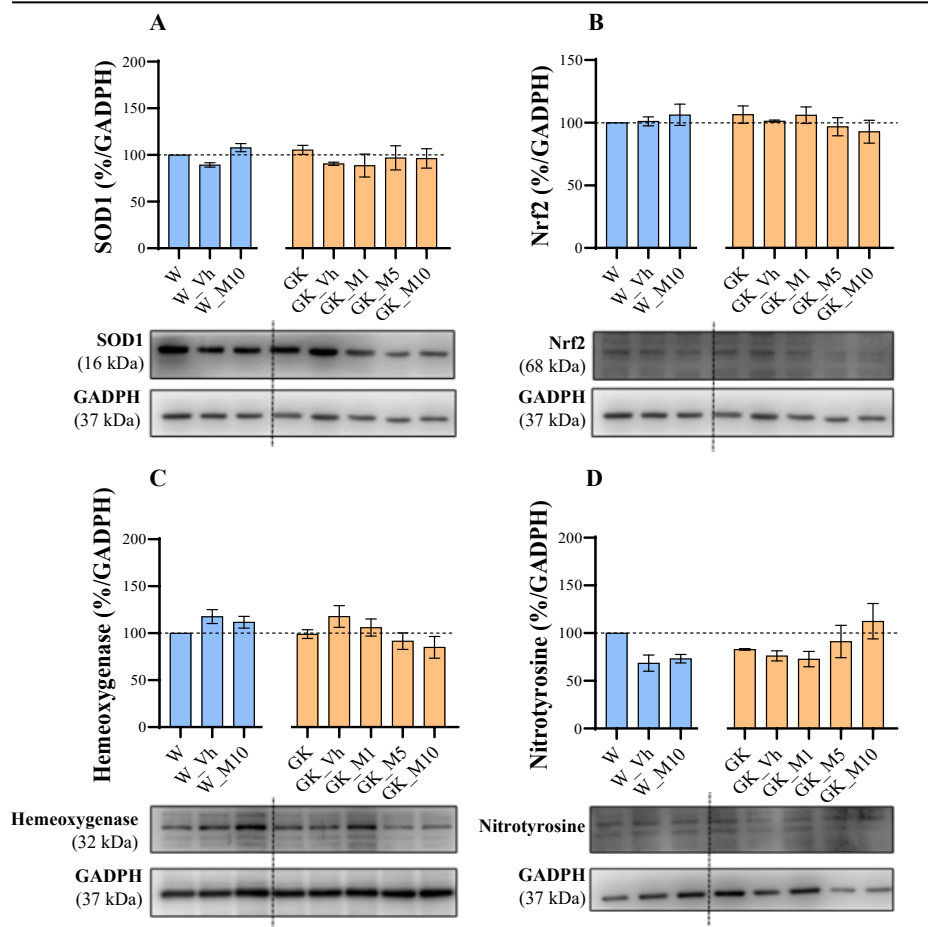


Figure S6: Effect of melanoxinet on the expression of SOD1 (A), Nrf2 (B), hemeoxygenase (C), and nitrotyrosine (D) in the heart. Results are expressed as mean ± SEM of 3 to 6 animals per group.

Aorta

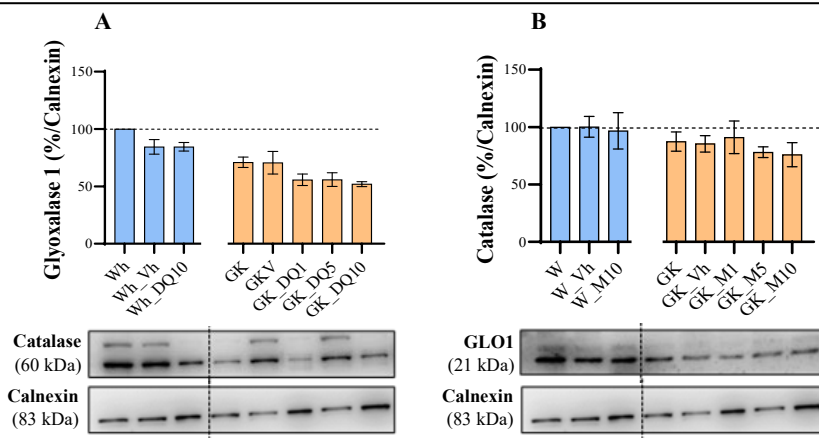


Figure S7: Effect of melanoxetin on the expression of GLO1 (A) and catalase (B) in the aorta. Results are expressed as mean \pm SEM of 3 to 6 animals per group.

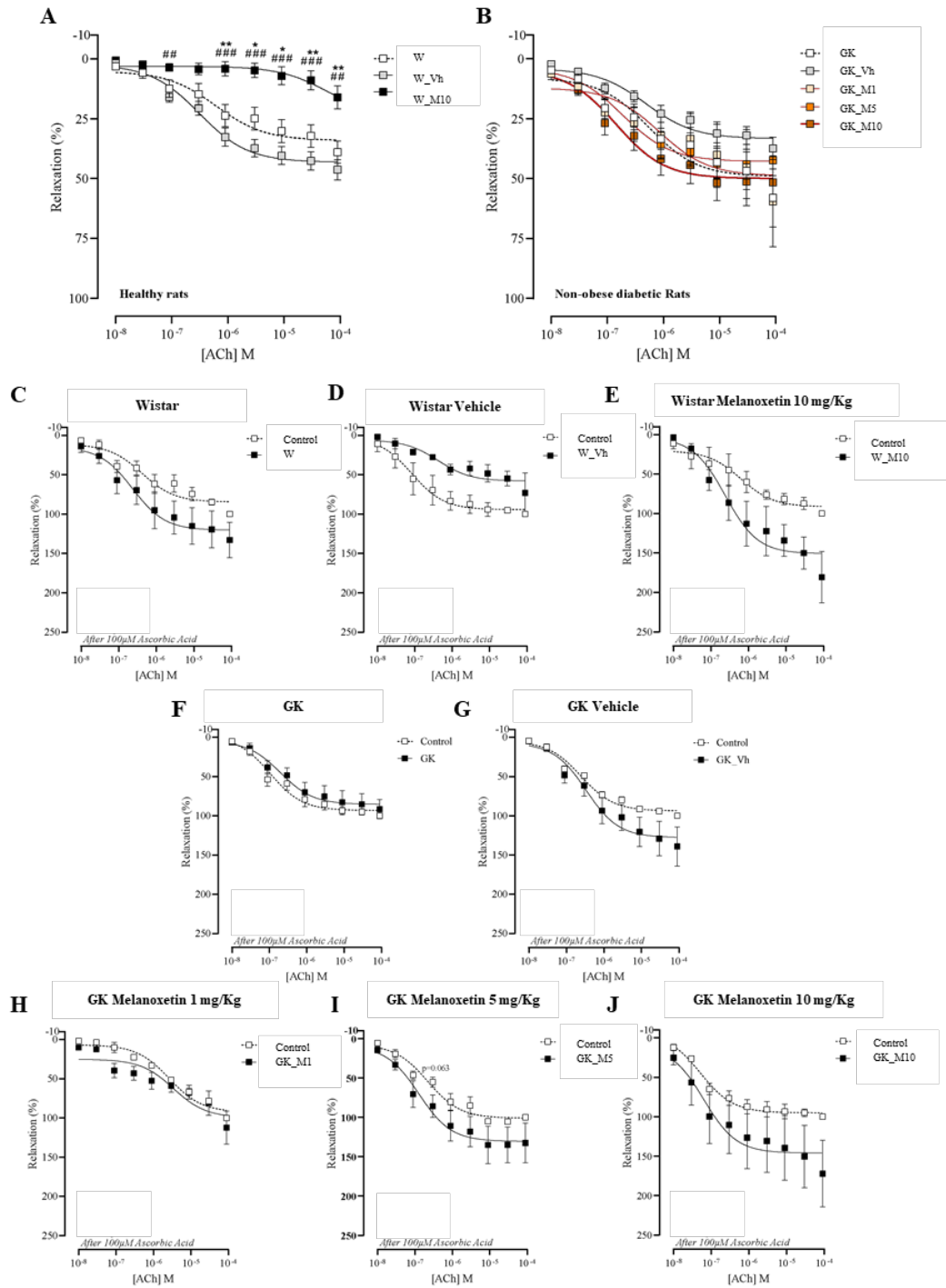


Figure S8: Effects of melanoxin treatment on relaxation response of the isolated to acetylcholine (ACh). The relaxation response was measured before (A and B) and after pre-incubation with ascorbic acid from Wistar control and Wistar vehicle rats (C and D), Wistar rats treated with 10mg/kg of melanoxin (E), GK control and vehicle (F and G) and GK rats administered with different concentrations of melanoxin - 1mg/kg, 5mg/kg and 10mg/kg (H, I and J).