

Supplementary Material

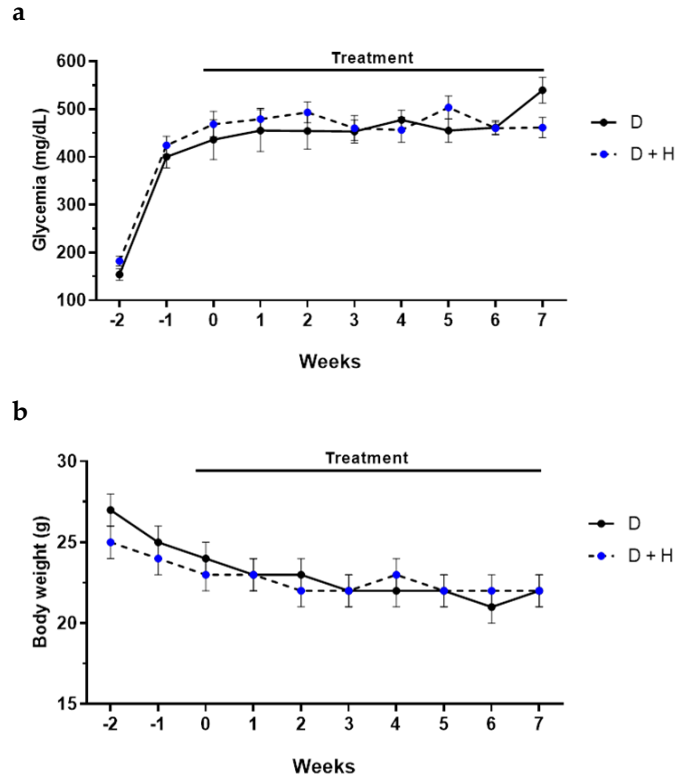
The synthetic flavonoid Hidrosmin improves endothelial dysfunction and atherosclerotic lesions in diabetic mice. Jimenez=Castilla et al.

SYBR Green Primers		
Gene (ID)	Forward	Reverse
<i>Nox1</i> (237038)	CCAACAGGCCATGGATGGAT	CACTCCAGTAAGCCAGCAA
<i>Nox4</i> (50490)	CCCTCCTGGCTGCATTAGTC	AACCCTCGAGGCAAAGATCC
<i>18S rRNA</i> (19791)	CCGTCGTAGTTCCGACCATAA	CAGCTTTGCAACCATACTCCC
Taqman Primers		
Gene	Assay ID	
<i>Ccl2</i>	Mm00441242_m1	
<i>Ccl5</i>	Mm01302428_m1	
<i>Il1-β</i>	Mm00434228_m1	
<i>Tnfα</i>	Mm00443258_m1	
<i>Sod1</i>	Mm01344233_g1	
<i>Cat</i>	Mm00437992_m1	
<i>Tert</i>	Mm00436934_m1	
<i>p16</i>	Mm00494449_m1	
<i>18s rRNA</i>	4310893E	

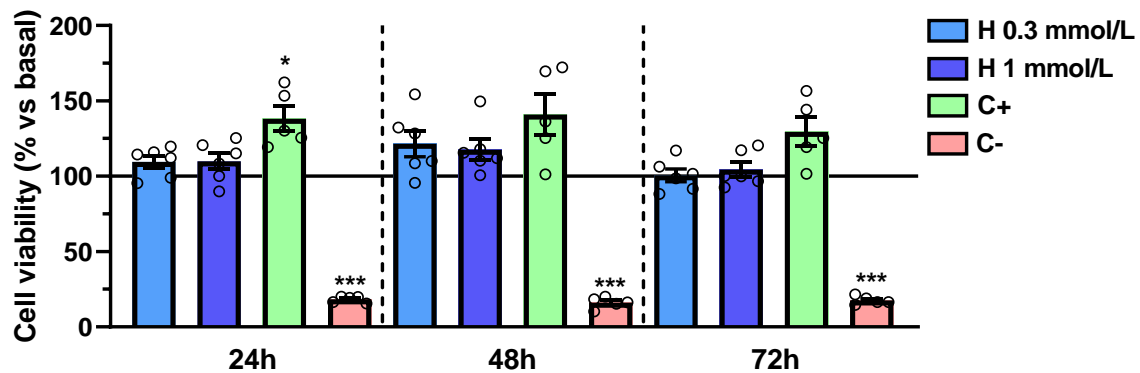
Supplementary Table S1. Mouse primers used for real-time qPCR.

Response			db/m	db/db	db/db +H
AORTA	Phe	EC50 (mM)	3.04±2.64	0.04±0.006 *	0.04±0.004*
		Rmax (mN/mm)	5.43±0.92	12.09±1.19*	12.76±0.95 *
	Ach	EC50 (mM)	0.14±0.03	0.41±0.19	0.07±0.02 #
		Rmax (%)	67.35±2.13	40.57±5.83 *	51.6±6.23
	DEA-NO	EC50 (mM)	0.69±0.06	0.63±0.08	0.77±0.22
		Rmax (%)	96.03±2.6	97.51±0.7	96.61±0.9
MRAs	Phe	EC50 (mM)	0.18±0.02	0.15±0.02	0.34±0.8 #
		Rmax (mN/mm)	2±0.16	1.8±0.17	1.6±0.26
	Ach	EC50 (mM)	0.029±0.009	0.472±0.231 *	0.013±0.003 #
		Rmax (%)	73.34±8.5	64.98±10	74.51±7.8
	DEA-NO	EC50 (mM)	0.6±0.4	0.19±0.06	0.27±0.08
		Rmax (%)	94.37± 1.9	96.67± 0.57	95.88 ±0.88

Supplementary Table S2. Summary of the measurements of vascular reactivity in the db/db mouse model. Values of half maximal effective concentration (EC₅₀) and maximum response (Rmax) to phenylephrine (Phe), Acetylcholine (Ach) and diethylamine NONOate (DEA-NO) in aorta and mesenteric resistance arteries (MRAs) segments from non-diabetic (db/m), untreated diabetic (db/db) and hidrosmin-treated diabetic (db/db+H) mice. **p*<0.05 vs. db/m and #*p*<0.05 vs. db/db by Kruskal-Wallis test followed by Dunn's post-test.



Supplementary Figure S1: Follow-up of metabolic parameters in diabetic ApoE KO mice. Evolution of glycemia (**a**) and body weight (**b**) of studied groups (untreated, D; hidrosmin treatment, D+H) after diabetes induction with STZ and during the treatment period. The graphs represent the mean \pm SEM of each group (D, n=7; D+H, n=11).



Supplementary Figure S2: Hidrosmin does not affect viability of VSMC. MTT viability assay in primary mouse VSMC incubated for 24, 48 and 72 h in medium with 0.5% FBS containing hidrosmin (H, 0.3 and 1 mmol/L), 20% FBS (positive control, C+) and 10% DMSO (negative control, C-). Bars represent the mean \pm SEM of 5-6 experiments analyzed in triplicate. * p <0.05 and *** p <0.001 vs. basal conditions (black line).