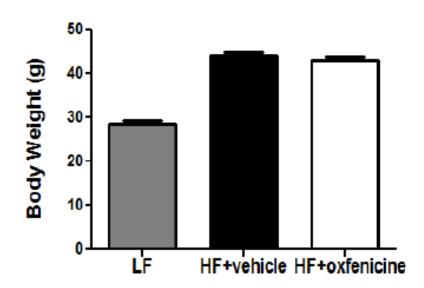
Supplementary Table 1. Effect of oxfenicine on body and tissue weight in high fat fed mice

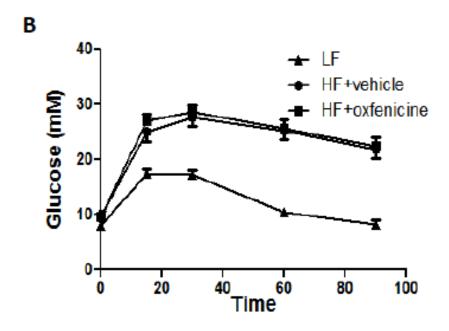
	HF	HF+oxfenicine
Body weight (g)	40±1.35	38.4±1.12
Epididymal fat (g)	1.63±0.09	1.58±0.11
Perirenal fat (g)	0.95±0.09	0.89±0.12
Heart weight/body weight	0.00104±0.00002	0.00113±0.00006
Liver weight (g)	1.49±0.19	1.28±0.10

Values represent mean  $\pm$  S.E.M. (n=6-8).

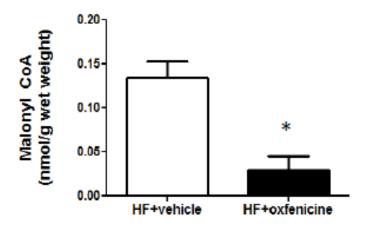
**Supplementary Figure 1.** Effect of high fat diet feeding on body weight and glucose tolerance in C57BL6 mice.A. Body weight and B. glucose tolerance test (GTT) of C57BL6 mice after 12 wks of HFD feeding before oxfenicine treatment. Values represent mean  $\pm$  SEM (n = 6-9). Differences were determined using a 2-way ANOVA followed by a Bonferroni post-hoc analysis. \*P<0.05, significantly different from the low fat diet mice.





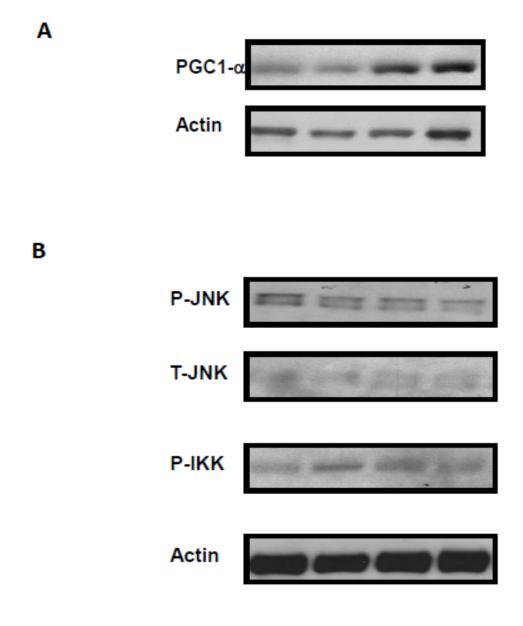


**Supplementary Figure 2.** Supplementary Figure 2. Treatment of HFD fed mice with oxfenicine results in inhibition of carnitine palmitoyltransferase 1 (CPT-1) activity in gastrocnemius muscles. Malonyl CoA levels in gastrocnemius muscles of HFD fed C57BL6 mice after treatment with vehicle or oxfenicine. Values represent mean  $\pm$  SEM (n = 6-9). Differences were determined using 2 –tailed Student's t test. \*P<0.05, significantly different from the low fat diet mice.



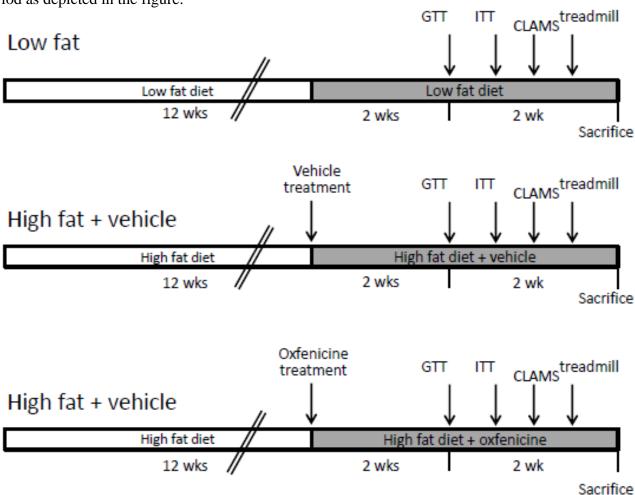
**Supplementary Figure 3.** Effect of oxfenicine treatment on the expression of various proteins in gastrocnmeius muscles of HFD fed C57BL6 mice.

A. Expression of PGC-1 $\alpha$  in gastrocnemius muscles of HFD fed C57BL6 mice after treatment with vehicle or oxfenicine. B. Phosphorylation status of IKK $\alpha$ / $\beta$  and JNK in gastrocnemius muscles of HFD fed C57BL6 mice after treatment with vehicle or oxfenicine.



# Supplementary Figure 4. Schematic of study design.

Mice were given a LF or HF diet for 12 wks after which HFD fed C57BL6 mice were treated with oxfenicine during the 4 wk period at 150mg/kg/day. Tests were performed during the 4 wk treatment period as depicted in the figure.



**Supplementary Figure 5.** Effect of oxfenicine treatment on glycogen metabolism in gastrocnemius muscles

A. Glycogen content in gastrocnemius muscles of HFD fed C57BL6 mice given vehicle or oxfenicine treatment. B. Phosphorylation status of GSK in gastrocnemius muscles of HFD fed C57BL6 mice after treatment with vehicle or oxfenicine.

Α

