Exogenous L-carnitine a meliorated burn-induced cellular and mitochondrial injuries of hepatocytes via recovering CPT1 activity

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Research

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Abstract

Background : Impaired liver fatty acid metabolism and persistent mitochondrial dysfunction are common phenomena and associated with liver failure. Decreased serum L-carnitine, a vitamin involved in fatty-acid and energy metabolisms, has been reported in severe burn patients. The current research aimed to study the effects and mechanism of L-carnitine on mitochondrial damage and other hepatocytic injuries.

Methods : Serum carnitine and indicators for hepatocytic injuries including AST, ALT, LDH, TG and OCT in severe burn patients and healthy controls were analyzed. The burn model in rats was established by skin scalding, and the carnitine was administered to the rats. The indicators mentioned above in the serum, and oil red staining, TUNEL staining and TEM observation, mitochondrial membrane potential, and CPT1 activity as well as CPT1 expression of the liver tissue were examined. HepG2 cells, treated with the CPT1 inhibitor etomoxir, were supplied with/without carnitine for 24h. The indicators mentioned above were examined, and apoptotic cells were analyzed by flow cytometry. Transcriptom high throughput sequencing of the rat liver tissues was performed, and differentially expressed genes Fabp4, Acacb, Acsm5 and Pnpla3 were further determined by RT-qPCR.

Results : Significantly decreased carnitine and increased AST, ALT, LDH and OCT in the serum were detected in the severe burn patients and the scalded rats. Accumulation of TG, obvious mitochondrial shrinking, altered mitochondrial membrane potential, decreased ketogenesis and declined CPT1 activity were found in the liver tissue of the scalded rats. Administration of carnitine recovered CPT1 activity and improved all the parameters for cellular, fatty acid metabolic and mitochondrial injuries. Inhibition of CPT1 activity with etomoxir in vitro induced similar hepatocytic injuries found in the burn patients and the scalded rats, and supplementation of carnitine restored CPT1 activity and ameliorated these injuries. Differentially expressed genes Fabp4, Acacb, Acsm5 and Pnpla3 in the liver tissue and in the etomoxir-treated hepatocytes were also restored by exogenous carnitine.

Conclusion : Exogenous carnitine exerts its protective effect on severe burn-induced cellular, fatty-acid metabolic and mitochondrial dysfunction of the hepatocytes via restore of CPT1 activity.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

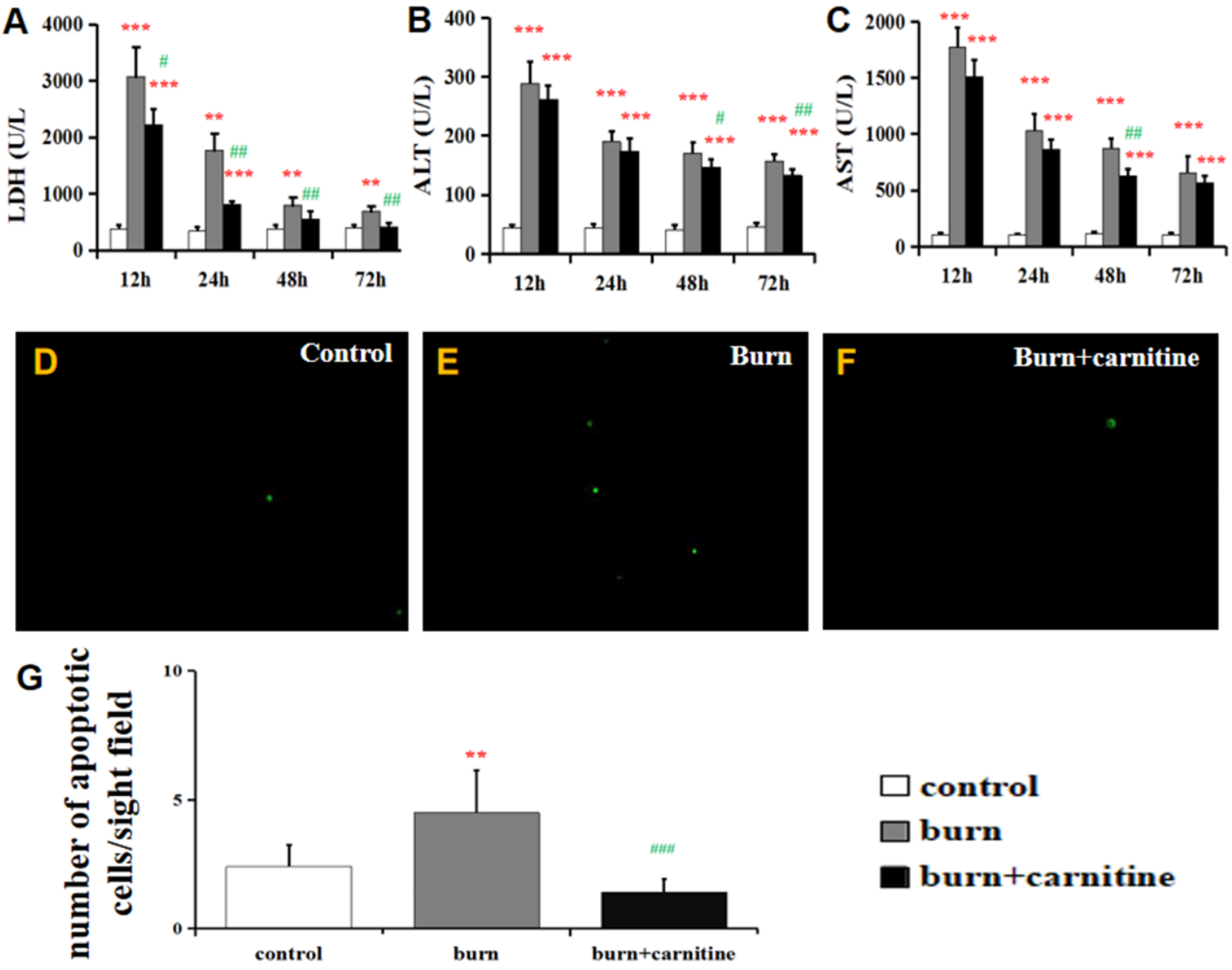

Figure 1

Effects of carnitine supplementation on hepatocytie injury in scalded rats Serum levels of LDH (A), ALT (B) and AST (C) in the control, burn and bum-lcamitine treated rats were detected. The representative images of TUNEL staining in the liver tissue of the control (D), burn (E) and burmlcarnitine (F) treated rats were showy Numbers of the positive cells of TUNEL staining in 10 randomly selected sight fields were represented in (G). The data are presented as mean + SD. **, P<0.01, ***, P<0.001, vs the control group: 0, P<0.05, P<0.01, and NW, F<0.001, vs the burn group.

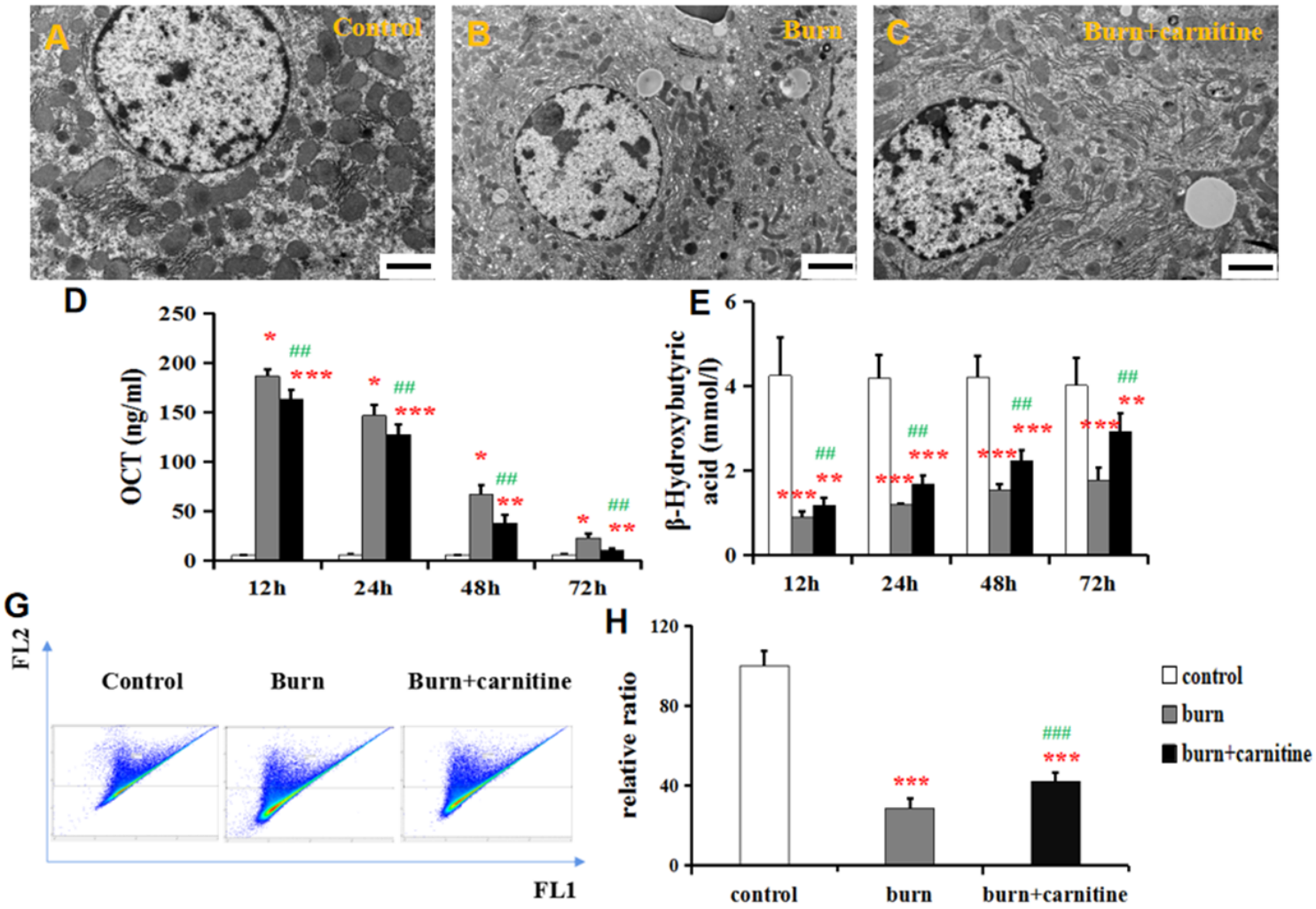

Figure 2

Effects of carnitine supplementation on mitochondria, injury of the Impatorytes in scalded rats. Representative images of transimshon electron microscopy of hepatocytes from normal (A), burn rats (B) and carmtmedreated bum rats (C) were shown Serum levels a OCT (0) and p■-118 (B) were indicated_ F 0 Changes of the milechondnal membrane potential (Aihm) m the hi/er tissues of the normal, burn and burnicarmtme rats were analyzed by flow cytometry as mtheated m (F), and relative mtrochondnal nxembrane potrnhals were expressed as 100%m the control. The data are presented as mean + SD. Y *. and 'B.* represeth FM0_05, 001 and 0001zespechvely, versus the control group, while MI represents P<001, the burnihamilme group versus th burn group

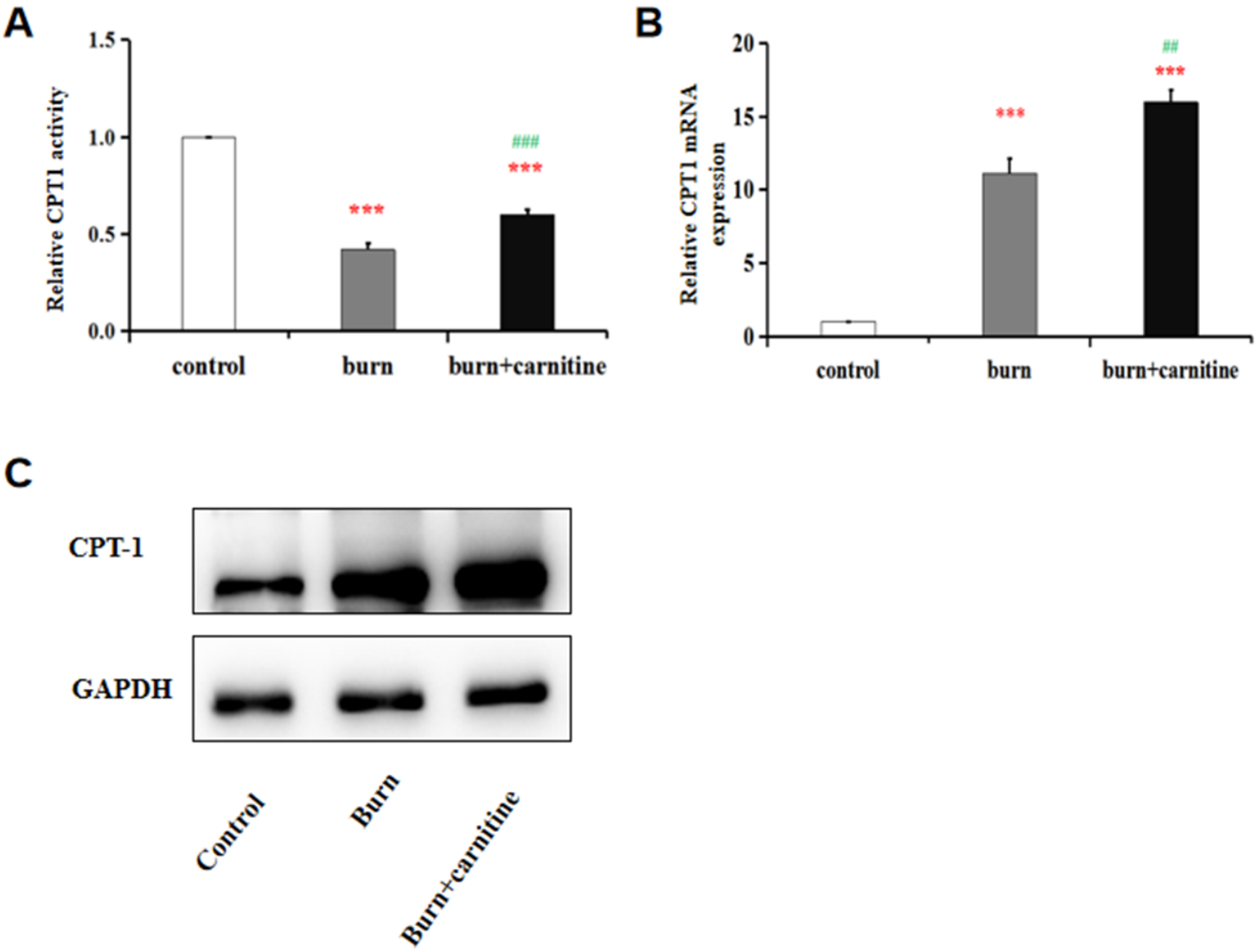

Figure 3

Changes of CPT1 activity and CPTIo mRNA expression in the rat liver tissues Relative roitochondrial CPT1 activities in the liver tissues of the rat 24 hours post the scalding were determined, and the control group was assigned as a value of 1 (A). Relative expression of CPT1 a chain mRNA m the rat liver tissues was assessed by RT-PCR (B). The data were represented as the meant SD; n=6 rats. *,** and *** represent P<0.05, 0.01 and 0.001,respectively, versus the control group, while #, 11# and ### represent P<0.05, 0.01 and 0.001,respectively, the bum+carnitine group versus the burn group.

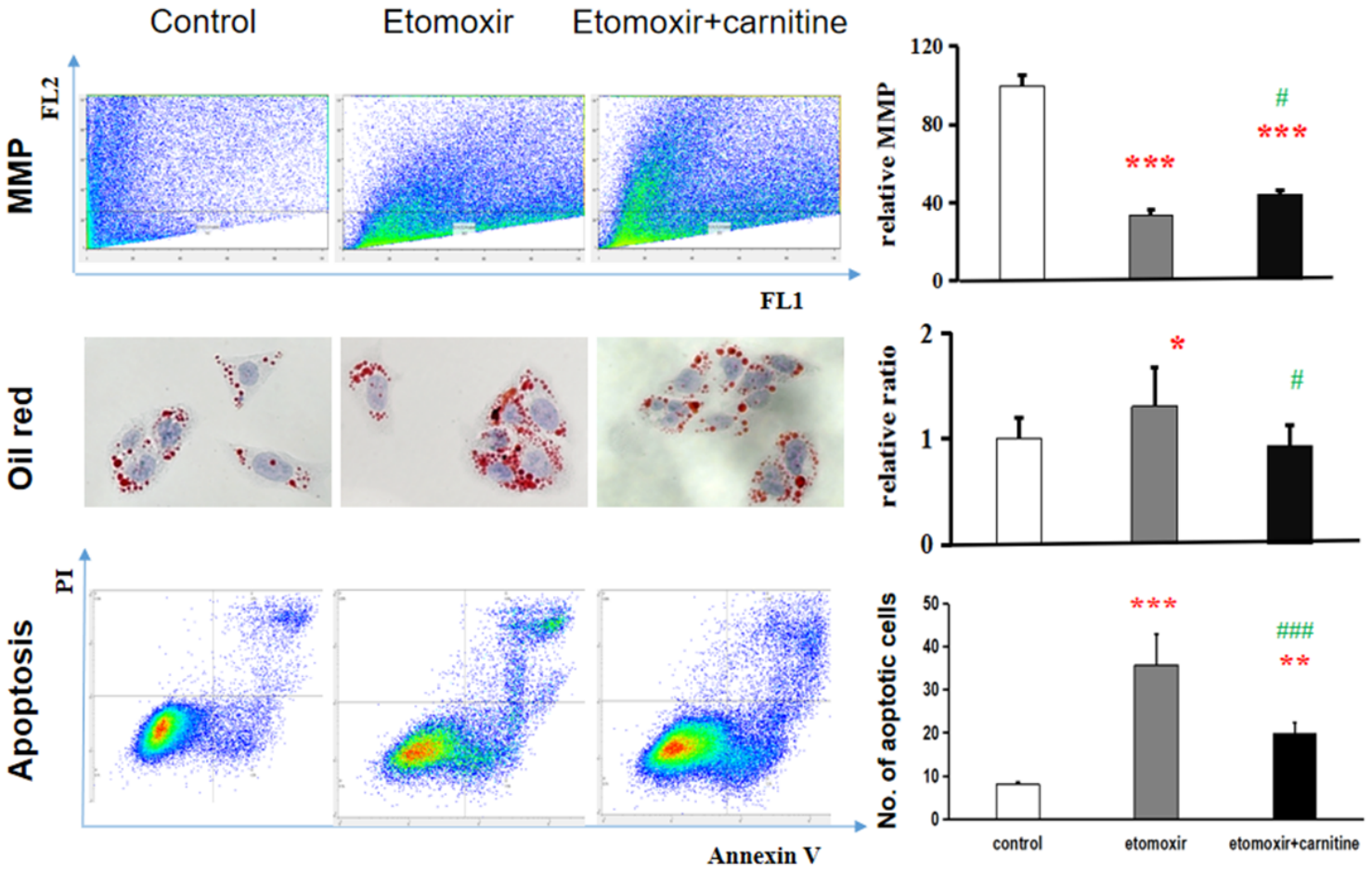

Figure 4

Effects of carnitine supplementation on mitochondria! membrane potential, lipid accumulation and apoptosis of HepG2 cells HepG2 cells were treated with or without 0.1 mM etomoxx or with without 0.1 mM etomoxir plus 0.2 mM L-camitine for 24h. Mitochondria) membrane potentials (MMP, in the upper of the left panel) were analyzed by JC-1 staining and flow cytometry, and the relative MMP was expressed in the upper of the right panel. TG accumulation was evaluated by oil rad staining (in the middle of the left panel), and the relative tensity was expressed in the middle of the right panel. Apoptotic HepG2 cells were stained with PI and annexin V and than analyzed by flow cytometry (in the lower of the left panel), and the number of apoptotic cells was shown in the lower of the right panel. The data were from 3 independent experiments and expressed as means # standard deviations (SD). * and *** represent P<0.05, and 0.001, respectively, versus the control group, while # and ### represent P<0.05 and 0.001, respectively, as the etomoxirTcarnitine group vs the etomoxir group.

Supplementary Files

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- SupplementaryMaterials.pdf