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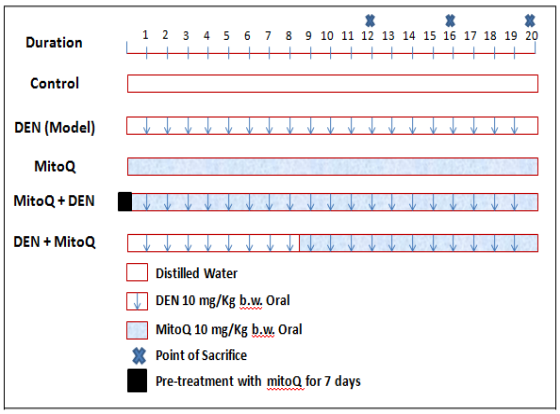
MITOQUINOL MESYLATE (MITO-MES) TARGETS MITOCHONDRIAL ANTIOXIDANT AND RESPIRATORY ENZYMES IN CIRRHOTIC AND HEPATOCELLULAR CARCINOGENIC RATS

ABSTRACT

Introduction:

Mitoquinol mesylate (Mito-MES) is a mitochondrial-targeted antioxidant that has been demonstrated to protect against several liver disorders. However, its role in cirrhosis and HCC remains unexplored, hence the present study investigated Mito-MES as a promising therapeutic for targeting mitochondrial antioxidant and respiratory enzymes to attenuate the progression of hepatocellular carcinoma (HCC) in Wistar rats.

MATERIALS AND METHODS:



Liver cirrhosis, early, and advanced HCC were induced in Wistar rats by oral administration of 10 mg/kg/day diethyl nitrosamine (DEN) for 12, 16, and 20 weeks, respectively. The cirrhotic, early, and advanced HCC rats were treated with Mito-MES (10 mg/Kg/day, oral gavage) as intervention therapy for 13, 17, and 21 weeks (pre-treatment) and 4, 8, and 12 weeks (post-treatment), respectively.

RESULTS:

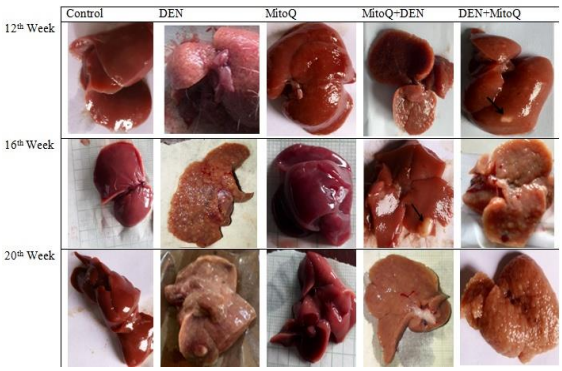


Plate 1: Effect of MitoQ on liver morphology of rats from each group at different stages of HCC; (12th week) Cirrhosis, (16th week) Early HCC, (20th week) Advanced HCC

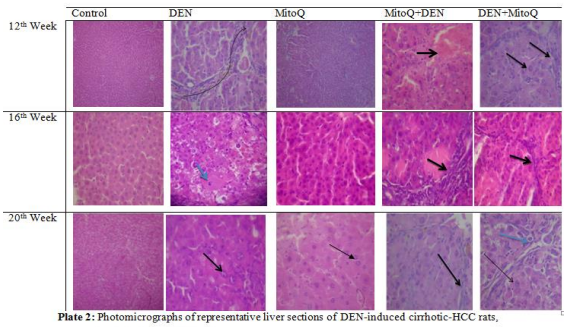


Plate 2: Photomicrographs of representative liver sections of DEN-induced cirrhotic-HCC rats, pre- and post-treated with MitoQ

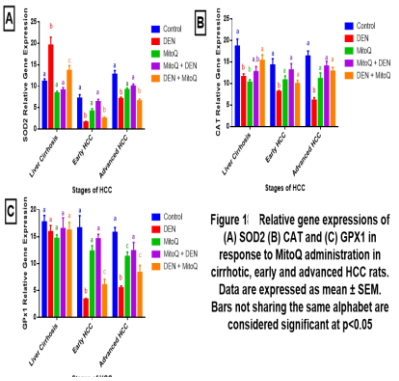
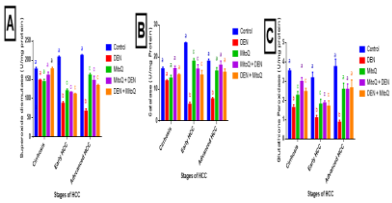


Figure 1: Relative gene expressions of (A) SOD2 (B) CAT and (C) GPX1 in response to MitoQ administration in cirrhotic, early and advanced HCC rats. Data are expressed as mean ± SEM. Bars not sharing the same alphabet are considered significant at p<0.05



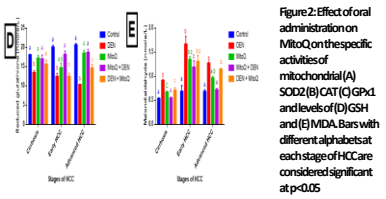


Figure 2: Effect of oral administration on MitoQ on the specific activities of mitochondrial (A) SOD2 (B) CAT (C) GPx1 and levels of (D) GSH and (E) MDA. Bars with different alphabets at each stage of HCC are considered significant at p<0.05

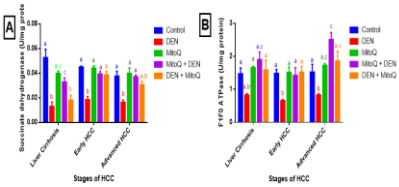


Figure 3: Effect of MitoQ on the specific activities of mitochondrial respiratory enzyme. [A] Succinate dehydrogenase [B] F1F0ATPase. Bars with different alphabets at each stage of HCC are considered significant at p<0.05

Mito-MES interventions inhibited the transformation of cirrhotic cells to malignancy and restored mitochondrial dysfunction induced by DEN-administration. Mito-MES achieved this promising effect by up-regulating the gene and protein expression of mitochondrial antioxidant proteins i.e. SOD2, GPX1 and CAT. Also, oral administration of Mito-MES increased the activity of mitochondrial succinate dehydrogenase and ATPase activity of F_1F_0ATPase in cirrhotic, early, and advanced HCC rats.

CONCLUSION: Mito-MES administration may represent a promising therapeutic for the prevention and treatment of liver cirrhosis and HCC