

The effects of alpha lipoic acid on damaged liver cells induced by n-6 polyunsaturated fatty acids in the young rats

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Nutrition is an important factor in the pathogenesis of several liver diseases [1]. Omega-6 fatty acids are essential for normal growth, development and health. It has been suggested that high dietary n-6 polyunsaturated fatty acids (PUFA) have differential effects on cell death and steatosis in the liver, but the mechanisms responsible for these differences are not known [2]. Alpha lipoic acid (ALA) (1,2-dithiolane-3-pentanoic acid), is a powerful antioxidant used in a number of conditions related to liver diseases [3]. In this study, the effect of alpha lipoic acid (ALA) on the liver cell damages and apoptosis by n-6 polyunsaturated fatty acids (PUFA) rich diet were examined.

Twenty four young Wistar albino rats (5 weeks old) were randomized two groups. During the fourth weeks 12 rats were fed with standart diet and other 12 rats were fed with contains n-6 high-fat diet. At the end of the fourth week each groups were randomly divided into two subgroups then ALA (35mg/kg, i.p.) was applied during four weeks period. (Groups;1.Control, 2.Control+ALA, 3.n6, 4.n6+ALA). At the end of the experiment, the animals were sacrificed. The level of tissue glutathione (GSH) activity was determined. The liver tissues were prepared for light microscopic (LM) and electron microscopic (EM) examination. Immunohistochemical staining was performed for caspase-3. Apoptotic cells were detected by TUNEL method. Caspase immunopositivity and fibrosis scores were detected using score technics, all values were analysed with statistical methods.

The GSH activity was significantly decreased ($p<0,001$) in liver tissue of n-6 group compared with the other groups. In the n-6 group cytoplasmic vacuolizations in the hepatocytes, mononuclear cell infiltrations and the increased collagen ($p<0,001$) around the central vein were observed by LM. TUNEL ($p<0,001$) and caspase-3 ($p<0,001$) positive cells were increased in n-6 group. In the n-6+ALA group, cytoplasmic vacuolizations, mononuclear cell infiltrations, apoptotic cells both in cell cordons and sinusoids were decreased according to the n-6 diet group and also increased GSH activity. Control+ ALA group was similar to the control group.

There were a number of hepatocyte filled with lipid droplets in their cytoplasm, degenerative areas containing apoptotic hepatocytes, a number of macrophages in the sinusoids and increased collagen fibers in n-6 group, whereas all degenerative observations were decreased in n-6+ALA group, also increased ITO cells containing many lipid droplets in the their cytoplasm were observed in the same group by EM. In conclusion, the present study results demonstrate that the feeding with n-6 PUFA causes fatty liver, fibrosis development, inflammations and apoptosis in the liver of young rats, ALA has a beneficial effects on these degenerative effects.

References

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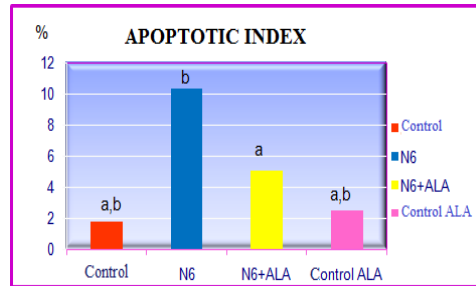


Table 1: The comparison of Apoptotic index for all groups. ^a $p < 0.001$ versus N6 group, ^b $p < 0.001$ versus N6 + ALA group

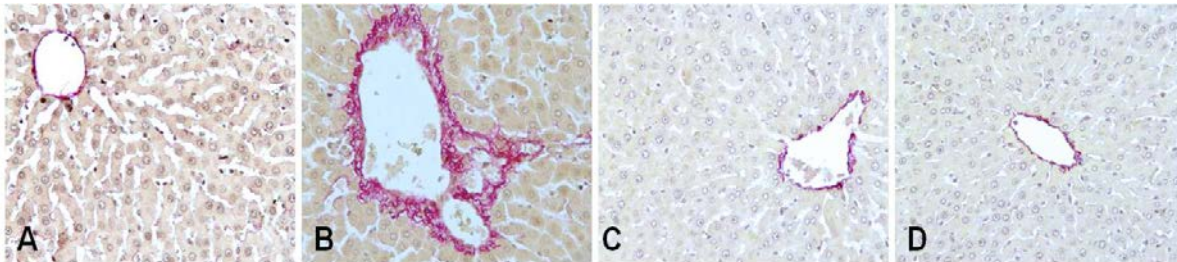


Figure 1. Sirius-red staining for collagen accumulation in all groups. (A:Control, B:n-6,C:n-6+ALA, D:Control+ALA groups) Magnification:X20

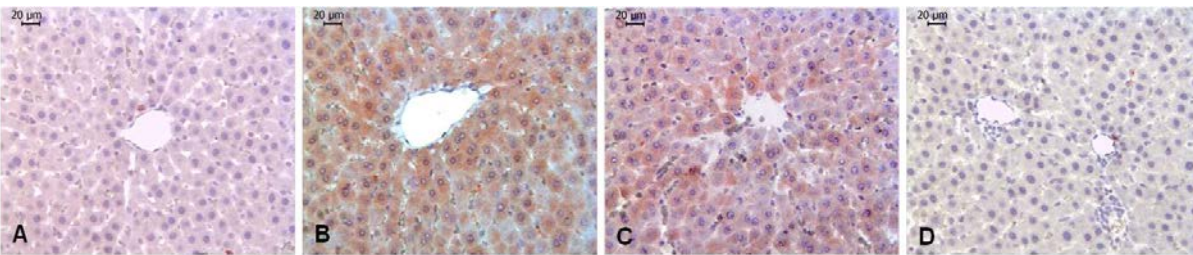


Figure 2. Immunolocalization of caspase-3 in liver of all groups.(A:Control, B:n-6, C:n-6+ALA, D:Control+ALA groups) Magnification:X20

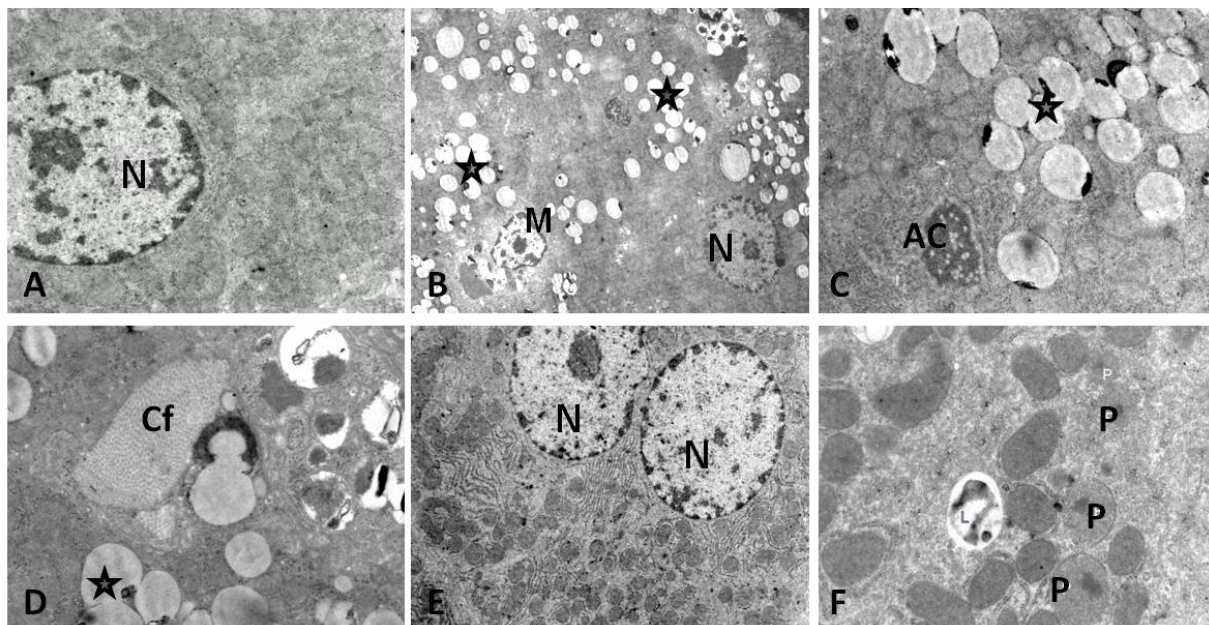


Figure 3: A: Control group. B-D: n-6 group, Hepatocytes containig lipid droplets (*) in the cytoplasm, apoptotic hepatocytes (AC), macrophages (M) in the sinusoids and increased collagen fibers (Cf) in n-6 group. E,F: n-6+ALA group, increased peroxisome (P) in hepatocyte. (N: Nucleus)