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# Comparative Histological, Immunohistochemical and Biochemical Study on the Effect of Vit. C, Vit. E, Gallic Acid and Silymarin on Carbon Tetrachloride Model of Liver Fibrosis in Rats

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**Abstract :** Background: Liver fibrosis is the main reason for increased mortality in chronic liver disease. It has no standard treatment. Antioxidants from a variety of sources are capable of slowing or preventing oxidation of other molecules. Aim: to evaluate the hepatoprotective effect of vit. C, vit. E and gallic acid in comparison to silymarin in the rat model of carbon tetrachloride induced liver fibrosis and their possible mechanisms of action. Material& Methods: A total number of 60 adult male albino rats 160-200gm were divided into six equal groups; received subcutaneous (s.c) injection for 8 weeks. Group I: as control. Group II: received 1.5 mL/kg of CCL4 .Group III: CCL4 and co- treatment with silymarin 100mg/kg p.o. daily. Group IV: CCL4 and co-treatment with vit. C 50mg/kg p.o. daily. Group V: CCL4 and co-treatment with vit. E 200mg/kg. p.o. Group VI: CCL4 and co-treatment with Gallic acid 100mg/kg. p.o. daily. Liver was processed for histological and immunohistochemical examination. Levels of AST, ALT, ALP, reduced GSH, MDA, SOD and hydroxyproline concentration were measured and evaluated statistically. Results: Light and electron microscopic examination of liver of group II exhibited foci of altered cells with dense nuclei and vacuolated, granular cytoplasm, mononuclear cell infiltration in portal areas, profuse collagen fiber deposits were found around portal tract, more intense staining α-SMA-positive cells occupied most of the liver fibrosis tissue, electron lucent areas in the cytoplasm of the hepatocytes, margination of nuclear chromatin. Treatment by any of the antioxidants variably reduced the hepatic structural changes induced by CCL4. Biochemical analysis showed that carbon tetrachloride significantly increased the levels of serum AST, ALT, ALP, hepatic malondialdehyde and hydroxyproline content. Moreover, it decreased the activities of superoxide dismutase and glutathione. Treatment with silymarin, gallic acid, vit. C and vit. E decreased significantly the AST, ALT, and ALP levels in plasma, MDA and hydroxyproline and increased the activities of SOD and glutathione in liver tissue. The effect of administration of CCl4 was improved with the used antioxidants in variable degrees. The most efficient antioxidant was silymarin followed by gallic acid and vit. C then vit. E. It is possibly due to their antioxidant effect, free radical scavenging properties and the reduction of oxidant dependent activation and proliferation of HSCs. Conclusion: So these antioxidants can be a promising drugs candidate for ameliorating liver fibrosis better than the use of the drugs and their side effects.

**Keywords :** antioxidant, ccl4, gallic acid, liver fibrosis
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