THE PROTECTIVE EFFECT OF SOME NATURAL PRODUCTS ON GENE EXPRESSION AND CHROMOSOMAL ABERRATIONS INDUCED BY THIOACETAMIDE IN MALE ALBINO RATS

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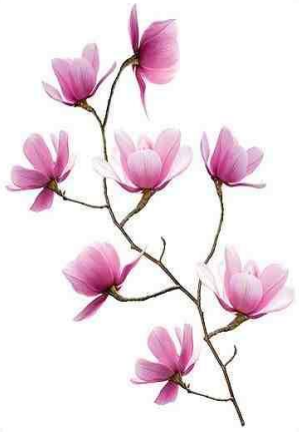

بسم الله الرحمن الرحيم

قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

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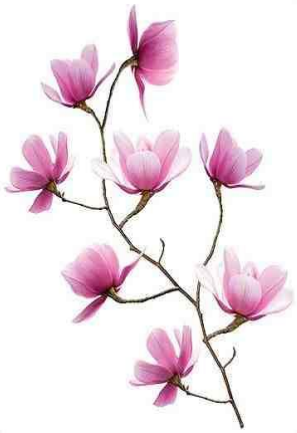

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جامعة عين شمس

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[شكـــر]

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ABSTRACT

The present study was oriented to explore the efficacy of *Boswellia serrata* extract and *Punica granatum* extract in the regression of liver fibrosis induced by thioacetamide (TAA) in male albino rats.

Sixty male albino rats 9-10 Weeks old, weighing approximately 150-170 g were divided into 6 groups. Group (1) was the normal control that received intraperitonial injection of 0.9 % normal saline solution (1ml / kg b. wt.) twice weekly for 7 weeks. , Group (2) in which the rats were intraperitoneally administered with (TAA) (200mg ⁄ Kg b.wt) twice weekly for induction of liver fibrosis, Group (3) in which the rats were orally treated with *Boswellia serrata* extract (175 mg ⁄ Kg b.wt) daily for 8 weeks, Group (4) in which the rats were orally treated with *Punica granatum* extract (400mg/kg b.wt) daily for 8 weeks . Group(5) in which rats were orally treated with *Boswellia serrata* extract (175 mg ⁄ Kg) after the injection with thioacetamide in a dose of 200mg ⁄ Kg b.wt twice weekly for seven weeks and Group(6) in which rats were orally treated with *Punica granatum* extract (400mg / kg) daily for 8 weeks after the injection with thioacetamide in a dose of 200 mg ⁄ Kg b.wt twice weekly for seven weeks .

Histological study of liver tissue, Bone marrow structural and numerical chromosomal aberrations investigation, were carried out. Also, Hepatic NQO1 and BCL-2 gene expression levels were detected. Liver enzymes (AST, ALT, and ALP), bilirubin, plasma fibrinogen and serum hepatocyte growth factor levels were

estimated. Hepatic reduced glutathione content was quantified. Furthermore, histological investigation of liver tissue of rats in Group (2) revealed many fibrotic features as inflammatory cells infiltration, fibroblastic cells proliferation, dividing the hepatic parenchyma into nodules and the formation of multiple numbers of new bile ductules. The TAA-treated group (group 2) showed significant increased in the number of structural chromosomal aberrations in bone marrow chromosomes such as fragment, ring form, deletion, centromeric attenuation, centric fusion and end to end association and numerical aberrations as polyploidy, significant down regulation ($P<0.05$) in hepatic NQO1 and BCL-2 gene expression levels, significant elevation ($P<0.05$) in the liver enzymes, bilirubin and hepatocyte growth factor were recorded versus the control group. Group (2) showed also a significant reduction in plasma fibrinogen level and hepatic reduced glutathione content.

In Group (3) and Group (4) there was an improvement compared to control in histological structure of liver, chromosomes, hepatic NQO1 and BCL-2 gene expression levels, liver enzymes (AST, ALT, and ALP), bilirubin, plasma fibrinogen, serum hepatocyte growth factor levels and hepatic reduced glutathione content compared with control group.

The study showed that Group (5) which received TAA then *Boswellia serrata* extract and Group (6) which received TAA then *Punica granatum* extract showed marked improvement compared to group (2) in the structural organization of the liver, in the number of the chromosomal aberrations relative to the TAA-treated group, also they revealed dramatic upregulation ($P<0.05$) in hepatic NQO1and BCL-2 gene expression levels, significant depletion ($P<0.05$) in serum liver enzymes activity and bilirubin, reduction in hepatocyte growth factor levels , significant

elevation($P<0.05$) in plasma fibrinogen level and significant increase in hepatic reduced glutathione content to near normal values in comparison with the TAA-treated group.

This study provided experimental evidences for the promising protective effect of *Boswellia serrata* extract and *Punica granatum* extract in amelioration of liver fibrosis, reduction of number of chromosomal aberrations, increasing in hepatic NQO1and BCL-2 gene expression, reduction in Liver enzymes (AST, ALT, and ALP) and bilirubin levels, increasing of Plasma fibrinogen level , reduction in serum hepatocyte growth factor levels and increasing in hepatic reduced glutathione content due to their hepatoprotective activity, antioxidant capacity and antifibrotic effect.

The results of the present study recommended that *Boswellia serrata* extract *and Punica granatum* extract shoud be used as curative agent respectively for liver fibrosis, chromosomal aberrations, NQO1and BCL-2 gene expression and Liver enzymes level .

Key words: liver fibrosis, *Boswellia serrata*, *Punica granatum*, antioxidant, antifibrotic , rats .

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