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**Protective Effect of Febuxostat on Lincomycin-Induced  
Hepatotoxicity and Nephrotoxicity in Rats**

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Submitted to Faculty of Veterinary Medicine Mansoura University  
For the PhD degree  
(Pharmacology)

**(2021)**

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## List of Abbreviations

<b>ALT</b>	Alanine aminotransferase
<b>ALP</b>	Alkaline phosphatase
<b>AST</b>	Aspartate aminotransferase
<b>RBC</b>	Red blood cell
<b>WBC</b>	White blood cell
<b>G+ve</b>	Gram positive
<b>Hb</b>	Hemoglobin
<b>H&amp;E</b>	Hematoxylin and eosin stains
<b>MDA</b>	Malinoldehyde
<b>MCV</b>	Mean corpuscular volume
<b>MCHC</b>	Meancorpuscular Hemoglobin concentration
<b>MCH</b>	Mean corpuscular hemoglobin
<b>SPSS</b>	Statistical Package for the Social Sciences
<b>NRC</b>	National Research Council
<b>PCV</b>	Packed cell volume
<b>n</b>	Number

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## **Summary**

The present study was conducted to investigate the ameliorating effect of Febuxostat, if any, on hematological profiles (erythrocytes, hemoglobin, PCV%, leucocytes and their differential count), liver function (AST, ALT, total protein, albumin and globulin), kidney function (urea and creatinine), antioxidant (malondialdehyde, catalase and reduced glutathione) and Histopathological effects on liver, kidneys and skeletal muscle.

Twenty-four apparently clinically healthy female albino wistar rats (200± 15g) were used. The albino rats were randomly divided into 4 groups as following:

- (G1) control and received distilled water.
- (G2) given lincomycin (500 mg/kg) orally by stomach tube for 10 successive days.
- (G3) given febuxostat (10 mg/kg) orally by stomach tube for 10 successive days.
- (G4) given lincomycin (500 mg/kg) plus febuxostat (10 mg/kg) orally by stomach tube for 10 successive days.

Blood samples were drawn from the retro-orbital plexus on the first, seventh and fourteenth days after the experimental periods from five rats from each group. After fourteen days of treatment, five rats were selected from each group, and samples of the liver, kidneys and skeletal muscles were collected for histopathological examination.

At fourteen days post treatment, five rats from each group were sacrificed by decapitation and specimen from liver, kidney and skeletal muscle were collected for histopathological examination.

The results showed the following:-

The obtained result showed that, lincomycin treated groups showed a non-significant decrease in total erythrocytic count and hemoglobin values at 1<sup>st</sup> and 7<sup>th</sup> days post dosing compared to the control group. While at 14<sup>th</sup> day after treatment a significant decrease in total R.B.Cs count and hemoglobin values were recorded in lincomycin treated group compared to the control group. Groups treated with febuxostat alone or in combination with lincomycin showed non-significant alterations in total erythrocytic count at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> day after treatment.

Regarding to PCV values in all treated groups, a non-significant decrease was recorded in lincomycin treated group compared with the other groups at 1<sup>st</sup> and 14<sup>th</sup> days after treatment. While the values of MCV, MCH and MCHC revealed non- significant differences within all treated groups.

The results also showed that the total leukocytic count at 1<sup>st</sup> day after treatment was non-significantly increased in lincomycin treated and febuxostat treated groups and a significant increase in group given a combination of lincomycin with febuxostat. At 7<sup>th</sup> day post dosing the total leukocytic count showed a non-significant decrease in lincomycin treated group and a non-significant increase in lincomycin with Febuxostat treated group. While at 14<sup>th</sup> day post treatment the group treated with lincomycin

recorded a non-significant decrease in W.B.Cs count in comparison with the control group.

The obtained data revealed that, neutrophils percent in lincomycin treated group showed a significant increase compared with the control group at 1<sup>st</sup> day after treatment. Febuxostat treated group and lincomycin with febuxostat treated group revealed a non-significant significant increase in neutrophils percent in comparison to the control group. While at 7<sup>th</sup> day after treatment there is a non- significant increase in neutrophil percent within all treated groups.

The results were illustrated that there was no significant decrease in lymphocytes and monocytes percentage in all treated groups at 1<sup>st</sup> and 7<sup>th</sup> days post treatment compared with the control group.

The results showed that, ALT values evoked a significant increase in lincomycin treated group in comparison to the control group at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> days after treatment. Also there is a non-significant increase in febuxostat treated group and lincomycin with febuxostat treated groups compared with the control group at 1<sup>st</sup> and 14<sup>th</sup> days after treatment.

The levels of AST were significantly increased in Lincomycin treated group at 1<sup>st</sup> day, 7<sup>th</sup> day and 14<sup>th</sup> days after treatment. Groups treated with febuxostat and lincomycin with febuxostat evoked a significant increase in AST levels at the 1st day post dosing in comparison to the control group.

The obtained results showed a highly significant increase in ALP levels of lincomycin treated group and a significant increase in ALP levels in febusostat treated group and in combination of lincomycin with febusostat treated group in compare with control group at 1<sup>st</sup> day post treatment. At 7<sup>th</sup> and 14<sup>th</sup> days after treatment, the levels of ALP were significantly increased in lincomycin treated group and lincomycin with febusostat treated group compared with the control group.

The obtained data revealed that, total protein level elicited a significant increase in febusostat treated group compared with the control group and the other treated groups at 1st day after treatment. The levels of total protein in febusostat treated group and in lincomycin plus febusostat treated group showed significant increase in comparison to lincomycin and control groups at 7<sup>th</sup> day post dosing.

Albumin level showed a significant increase in febusostat treated group compared with the control group at 1<sup>st</sup> and 7<sup>th</sup> days after treatment. All treated groups elicited a non-significant difference in the levels of serum albumin at 14<sup>th</sup> day after treatment compared with the control group.

The levels of serum globulin showed a significant increase in febusostat treated group compared with the control group at 1<sup>st</sup> and 7<sup>th</sup> days after treatment. At 14<sup>th</sup> day post treatment, all treated groups evoked a non-significant difference in the levels of serum globulin compared with the control group.

The recorded results revealed that, the levels of urea evoked a highly significant increase in serum of lincomycin treated group compared with the

control group at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> days after treatment. Also there is a significant increase in serum urea level of lincomycin with febuxostat treated group in compared to febuxostat treated and control groups at 1<sup>st</sup> and 7<sup>th</sup> days after treatment but significantly decreased in comparison with Lincomycin treated group at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> days post treatment.

The results showed that, the creatinine levels revealed a significant increase in serum of lincomycin treated groups in comparison with the control group at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> days after treatment. There is a significant decrease in creatinine level in serum of lincomycin with febuxostat treated groups compared to the lincomycin treated group followed by control groups at 7<sup>th</sup> day post dosing.

Our result elicited a significant decrease in serum catalase levels in of all treated groups (Lincomycin, Febuxostat and their combination) compared with the control group at 1<sup>st</sup> day after treatment. Also, at 7<sup>th</sup> day post treatment, there is a significant decrease in serum catalase level of lincomycin treated group in comparison with the control group. While non- significant differences between all compared groups at 14<sup>th</sup> day after treatment were recorded.

The obtained data evoked a significant decrease in serum MDA levels of group treated with combination of lincomycin with febuxostat compared to the other treated groups at 1<sup>st</sup> day post dosing. However there is a significant increase in serum MDA levels of lincomycin treated group in compared to other treated groups at 7<sup>th</sup> day after treatment. On the other hand, non-

significant differences were noticed between all treated groups at 14<sup>th</sup> day post treatment.

Reduced glutathione levels recorded a significant increase in serum of lincomycin treated group and a significant decrease in serum of group given lincomycin with febuxostat at 1<sup>st</sup> day post dosing compared to the control group. While there are no significant differences in serum reduced glutathione levels between all treated groups at 7<sup>th</sup> and 14<sup>th</sup> days after treatment.

Renal sections from group received lincomycin showing marked tubular dilation, cast formation dilated Bowman's capsule and multifocal interstitial leukocytic cells aggregation in cortex with congested capillaries in medulla, while renal sections from group received combination of lincomycin and febuxostat showing improved histological picture with mild dilation of few cortical and medullary tubules.

Hepatic sections from group received lincomycin showing diffuse hydropic degeneration of hepatocytes with bile retention while hepatic sections from group received combination of lincomycin and febuxostat showing improved histological picture with mild vacuolar degeneration in few hepatocytes around central veins.

Skeletal muscular sections from group received lincomycin showing severe hyalinization of many longitudinally and crossly sectioned muscle fibers manifested by more eosinophilic and structure-less sarcoplasm while skeletal muscular sections from group received lincomycin with febuxostat retained relatively normal histological picture of longitudinally) and crossly sectioned muscle fibers.