Effect of Taurine on hematological disturbance towards carbon tetrachloride hepatotoxicity in mice

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Abstract Background: Hepatic damage caused by chemicals is associated with distortion of the metabolic functions and may lead to progressive liver fibrosis, ultimately cirrhosis, and hepatocellular carcinoma. This study was carried out using Taurine (TAU), and was applied on 60 swiss male adult albino mice. The results revealed that TAU was efficient against carbon tetrachloride (CCl_4) hepatotoxicity in the studied groups. It could ameliorate hematological changes caused by CCl_4 toxicity by decreasing white blood cells and increasing platelets, red blood cells, Hemoglobin concentration and hematocrit values. Conclusion: TAU could ameliorate hematological disturbance caused by CCl_4 toxicity.

Index Terms: Hepatotoxicity; Carbon tetrachloride; Taurine; Complete blood count; hematological disturbance

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Abbreviations

Hematocrit	HCT
Hemoglobin	HGB
Platelets	PLT
Red blood cells	RBCS
Taurine	TAU
White blood cells	WBCS

1. INTRODUCTION

CCl4 has been widely studied as a hepatotoxic agent [1]. Hepatotoxicity of CCl4 involves its biotransformation into free radicals such as trichloromethyl free radical (·CCl_3) and trichloroperoxyl radical (.$OOCCl_3$) and increased lipid peroxidation [2]. Free radicals have the potential to covalently bind to large molecules such as lipids, proteins, and nucleic acids. The double allylic hydrogen bonds of polyunsaturated fatty acid are vulnerable to be attacked by free radicals [3]. Taurine, 2-aminoethane sulfonic acid, is the second most abundant amino acid after glutamate in the central nervous system of mammals. Taurine is synthesized from the metabolism of methionine and cysteine mainly in liver and brain [4]. Taurine contributes in several physiological functions in mammalian cells, such as osmoregulation, anti-inflammation, membrane stabilization, ion transport modulation, regulation of oxidative stress and mitochondrial protein synthesis [5]. Taurine is known to improve cellular antioxidant defense system, stabilize bio-membranes and reduce in vivo lipid peroxidation (LPO), thus preventing apoptosis and necrotic cell death [6]. The effect of Taurine on cell mitochondria is reported in several investigations. Taurine regulates mitochondrial pH, affects mitochondrial GSH and antioxidants, and preserve the mitochondrial membrane potential [7]. The protective effects of taurine against carbon tetrachloride (CCl_4) induced oxidative stress, which cause liver damage. In addition, the protective effects of taurine against cytotoxicity and oxidative stress have been observed not only in hepatocytes, but also in other cells and tissues, both in vivo and in vitro [8]. Taurine has been considered for the treatment of a wide range of disease including epilepsy, diabetic complications, and cardiovascular disorders. Taurine has also been shown to protect against hepatotoxicity induced by either tamoxifen [9] or acetaminophen [10].

The present study investigate the effect of taurine towards hematological alternations associated with CCl4 hepatotoxicity.

2. MATERIALS AND METHODS

2.1. Chemicals

TAU was purchased from Sigma-Aldrich Chemical Co., (St Louis, MO, USA). CCl_4 was purchased from BDH Chemicals, Ltd, Poole, England.

2.2. Animals:

2.2.2. Experimental Animals

60 adult male Swiss albino mice weighing (25-30g) housed at experimental animal house of the Faculty of Science, Damietta University. The animals maintained in controlled environment of temperature, humidity, light and fed on a commercial standard diet and tap water *ad libitum.*

2.2.3. Experimental design

60 Swiss male adult albino mice divided into 4 groups (15 mice/each) as follow: Group I served as negative control was given 0.5 ml olive oil/kg b.w. intraperitoneally (i.p.) for 5 weeks; Group II positive control (CCl_4 group) recived CCl_4 1 ml (50% in olive oil)/kg b.w. (i.p.) 3 times a week for 5 weeks, Group III (Taurine treated group) (CCl_4+TAU) mice received CCl_4 as group II followed by TAU for one month more; Group IV (Taurine control group) mice was injected with TAU for one month. At the end of the experiment, animals weighed then anesthetized under light ether and dissected. Blood samples were collected for hematological analysis.

2.3. Complete blood count (CBC)

Portion of retro orbital blood samples collected of each animal used for complete blood count. Blood cell counts performed with HORIBA Hematology analyser (France).

2.4. Statistical analysis: *Data evaluated by one-way analysis of variance (ANOVA) by"SPSS" 14.0 for Microsoft Windows, SPSS Inc. and considered statistically significant at a two-sided $P < 0.05$. Numerical data expressed as mean ± SD.*

3. RESULTS

3.1. Effect of taurine on hematological changes in all studied groups:

Treatment with CCl_4 significantly increased the numbers of white blood cells (WBCs) to (20.37+2.1 x 103/mm3), reduced platelets count to (535+27.06 x 103/mm3), Red blood cells (RBCS) levels to (6.35+ 0.28 x106/mm3), Hematocrit levels to 27.54+1.5%, ($p<0.001$) and Hemoglobin concentration to 9.71+ 0.69 g/dl, ($p<0.05$) in the blood compared to control group (13.21+1.7 x 103/mm3, 645.42 + 61.27 x 103/mm3, 6.73+0.35 x106/mm3, 31.31+0.9, 31.31+0.9, ($p<0.001$),and 10.77+1.6, ($p<0.05$)) respectively. On the other hand; white blood cells significantly decreased in taurine group, ($p<0.001$) compared to CCl4 group. platelets counts ,Hemoglobin concentration, red blood cells and hematocrite counts significantly increased by taurine compared to CCl4 group as shown in Table 1 .

TABLE 1: EFFECT OF TAURINE ON WBCS,RBCS PLT,HGB AND HCT COUNTS IN ALL STUDIED GROUPS

Group	WBCS x(10^3/mm^3) Mean ±SD	RBCS x(10^6/mm^3) Mean ±SD	PLT x (10^3/mm^3) Mean ±SD	HGB (g/dl) Mean ±SD	HCT% Mean ±SD
Negative control	13.21±1.7	6.73±0.35	645.42±61.27	10.77±1.6	31.31±0.9
CCl_4 control	20.37±2.1[a]	6.35±0.28[a]	535±27.06[a]	9.71±0.69[a*]	26.54±1.5[a]
TAU group	13.2±1.6[b]	6.95±0.61[b]	882.28±76.46[b]	10.57±0.65[b*]	31.89±0.91[b]
TAU control	8.15±1.85	6.94±0.60	987.85±186.81	10.37±0.51	33.94±0.68

Results expressed as mean ± SD. (a) Compared with normal control. (b) Compared with CCl4 control. Highly significant difference from control value at (P<0.001). (*) significant difference from control value at (P<0.05).

4. DISCUSSION

Antioxidants are natural or synthetic compounds, produced in vivo, normal cell constituents, or delivered in diets, whose main function is to fight against oxidative stress [11], being thus able to either delay or prevent the oxidation of substrates, such as proteins, deoxyribonucleic acid (DNA), lipids, DNA mutations, malignant transformations, as well as other parameters of cell damage [12]. Among our study, obtained data showed a significant decrease in the hematocrit values and platelets counts, red blood cells, a significant increase in the number of WBCS (p<0.001), and a significant decrease in hemoglobin concentration in CCl_4 group(p<0.05), compared with the control group. These results were in agreement with Abdel-Bakky [13] who said that CCl_4 treatment resulted in a significant reduction in platelets and elevation in WBCs counts. While, there were a significant increase in hematocrit values, red blood cells, platelets counts (p<0.001), and hemoglobin concentration (p<0.05) in taurine treated group compared to CCl_4 group, and in taurine control group compared to normal control group. On the other hand there were a significant reduction in WBCs counts due to taurine treatment (p<0.001), compared to CCl_4 group. In taurine control group, there were an increase in hematocrit values, red blood cells, platelets counts, and a reduction in WBCs counts compared to normal control and CCl_4 groups. It is interesting that in pervious study of Sidrah [14], who demonstrated the feasibility of adding taurine as an antioxidant to whole blood collected in K3-EDTA tubes which exhibited different patterns of reliability on CBC parameters over time.

5. CONCLUSION

In conclusion, Treatment with taurine ameliorates the hematological disturbance induced by CCl_4 in mice. In the light of our results, this may be attributed to the antioxidant effects of taurine.

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