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PARACETAMOL OVERDOSE;

ROLE OF TRIFOLIUM EXTRACTS ON THE LIVER FUNCTIONS OF PARACETAMOL OVERDOSE IN RABBITS.

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ABSTRACT… Background: Liver plays a central role in the process of metabolism, storage of glycogen and detoxification. It acts as major organ in the physiologic role of body. Paracetomol is oftenly used as a pain reliever and antipyretic, its overdose can liver toxicity and produces free radicals which is dangerous for human health. **Objectives:** To find the role of trifolium extract in the limitation of hepatotoxicity instigate by paracetamol overdose. **Study Design:** Cross sectional Study. **Setting:** Pathology Department, Post Graduate Medical Institute (PGMI) Lahore. **Period:** April 2016 to October 2016 for the period of 6 months. **Material and Methods:** Total 32 rabbits were taken for the study. They were divided into four groups. Group I was control, group II, III, IV were intoxicated with paracetamol dose 1, 1.5, 2 g/kg body weight respectively. Each group was composed of 8 rabbits. Each paracetamol intoxicated rabbit was treated with triflolim extract for 5 days. **Results:** Paracetamol overdose causes a significant raise in the liver functions eg alanine aminotransferase (ALT), Asparate aminotransfearse (AST) alkaline phosphatase (ALP) and total bilirubin (T. bilrubin). There is remarkable improvement in the liver functions when the intoxicated rabbits were treated with triflolium extract. **Conclusion:** Triflolium extracts has better results and can limits the damaging effects of paracetamol overdose on liver functions.

Key words: ALP, ALT, AST, T.bilrubin, Paracetamol, Trifloium Extracts.

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INTRODUCTION

Hepatoxicity caused by drug has been established because liver play an important role in drug metabolism. Paracetamol is commonly used for analgesia and as an antipyretic. It is metabolized in the liver by sulfonation, oxidation and glucuronidation.[1] The process of oxidation produces n-acetyle-p-benzoquinoneimine (NAPQI) which is a reactive arylating agent. This agent bound to the glutathione in balanced form. Glutathione is antioxidant agent which detoxifies the hepatocyte toxicity and it is produced by the liver cells. When the formation of NAPQI is greater than glutathione then toxicity of hepatocytes occurs. This deteriorates the hepatic functions which is required for physiologic drug metabolism.[2'3]

The metabolism of paracetamol in liver produces reactive oxygen species (ROS) in the form of free radicals by reduction of oxygen molecule. These free radicals damages cell mitochondria and alter the liver functions by affecting the hepatocytes. The intake of paracetamol should not exceed 4g/day because it can lead to hepatic failure.[4,5]

Trifolium belongs to the clover species family. It has the antioxidant, scavenging free radicals qualities. This herb extracts has been used in the folks medicine. It prevents lipid peroxidation and free radical formation in the liver toxicity induced by the paracetamol overdose. Plants extracts are commonly used in the diseased liver. The extracts of herbs are also used in the prevention of diabetes and atherosclerosis.[6,7] there is no such report has been published in Pakistan that trifolium extract can limit the liver damage and brings the liver parameters toward normal. Therefore the present was planned to find out the hepatoprotective role of trifolium extracts against the paracetamol

induced liver functions deterioration in rabbits.

MATERIAL AND METHODS

The study was conducted at Pathology Department Post Graduate Medical Institute (PGMI) Lahore from April 2016 to October 2016 for the period of 6 months. The rabbits were collected from the animal house of the PGMI. Total 32 rabbits were taken for the study. Paracetamol and trifolium extract were purchased by the institute and received from the store of PGMI. The reagent kits for ALT, AST, ALP and T.bilrubin were purchased from Abbot Company in Lahore. rabbits were divided into four group(I,II,III,IV), in each group eight(8) animals were included. Group I was control. 3ml blood sample was taken from the control and serum was stored at -4c for analysis. Then paracetamol dose was given to each group 1, 1.5, and 2 g/kg body weight respectively. Then each intoxicated group was treated with trifolium extract for 5 days. After 5 days 3ml blood sample was taken in sterile syringe, centrifuged and serum was taken and stored at -4c till the start of analysis. After collecting the entire sample the serum of each group was analyzed for liver functions tests (ALT, AST, ALP, T.bilrubin level) by autochemistry analyzer. The results were recorded for statistical analysis.

STATISTICAL ANALYSIS

All data were analyzed by using analysis of variance (ANOVA) and SPSS 20. The data was put in SPSS software for variable analysis. P ≤0.05 was considered significant. Data was presented as mean ± standard deviation of the mean (SD).

RESULTS

The results were expressed in the Table-I and II. Table-I shows all the groups of rabbits were given the dose of paracetmol according to their weight and their liver function alteration. In Table-II the values of liver analytes were expressed after the trifolium extract administration.

P ≤0.05 was considered significant for ALT, AST, T.bilrubin and ALP level by comparing paracetomol intoxicated rabbits with the extract administration.

Variable	Control I	Group-II 1g/kg	Group-III 1.5g/kg	Group-IV 2g/kg
T.bilrubin	0.1±0.02	1.2±0.1	2.1±0.02	2.7±0.03
ALT	45±2.5	70±2.5	80±2.81	101±4
AST	38±2.5	79±2.5	91±3.2	121±3
ALP	128±4	141±4	208±7.7	289±5.5
Total	8	8	8	8

Table-I. Liver functions of control and all the groups intoxicated with paracetamol P≤0.05

Variable	Control I	Group-II	Group-III	Group-IV
T.bilrubin	0.1±0.02	1±0.03	1.8±0.04	2±0.08
ALT	45±2.4	60±3.5	67±3	80±3.3
AST	38±2.2	69±4	77±2.8	99±3.9
ALP	128±5	137±5.5	167±6.8	200±7
Total	8	8	8	8

Table-II. Liver functions after t.extract administration P≤0.05

DISCUSSION

In the present study the results of liver function tests ALT, AST, ALP and Total Bilrubin were elevated compared to control values after administration of paracetamol, similarly according to (larrey et; al, 2015) the level of total serum bilirubin was also found to be increased significantly as a result of paracetamol overdose. Increase in the level of liver enzymes can cause the loss of cell membrane integrity and leads to the leakage.[8]

In murugaian et al; 2010) It has been proposed that over dose of paracetamol causes increased production of free radicals. These reactive oxygen species are responsible for hepatocyte death, mitochondrial dysfunction, fatty liver formation, lipid peroxidation and ultimately liver cell damage.[9] our study also says that paracetamol over dose causes alteration in liver enzymes and increases the level of total bilrubin as well. In this study paracetamol intake can cause hepatotoxic effects by cumulative oxidative damage mechanisms. The upper level of liver parameters brought to near normal limit after the administration of trifolium extracts for 5 days. It protects the hepatocytes by stabilizing the cell membrane integrity against paracetamol.[10,11,and12]

Trifolium flower hexane extract had the most protective effect against paracetamol toxicity. These results may be attributed to natural antioxidants in plants are usually fat soluble vitamins like vitamin A, ascorbic acid E and polyphenols.[13,14,15]

CONCLUSION

From the results it has been concluded that trifolium extract have protective role in the liver injury induced by the paracetomol overdose. It helps in bringing the liver functions tests to the normal limit and can reduce the liver damage.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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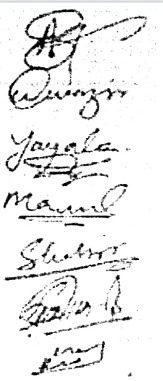
1	Muhammad Asif	Study design.	
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