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ORIGINAL ARTICLE

Effect of Corn Silk extracts on Hepatic steatosis in doxorubicin treated Albino Rats.

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ABSTRACT… Objectives: To determine hepatoprotective effects of cornsilk extracts through laboratory and histopathological parameters in albino rats. **Study Design:** Experimental Animal study. **Setting:** Animal House and Histology Laboratory of Postgraduate Medical Institute (PGMI) Lahore. **Period:** April 2019 to April 2020. **Material & Methods:** The study was carried out on 30 albino rats and was divided among three groups having ten rats in each group. Group A was labelled as a control group. Groups B and C were labelled as experimental groups. Cellular steatosis as a histological parameter and ALT and AST levels are measured to access the hepatoprotective effects of corn silk. **Results:** It was found that the mean AST and ALT were also significantly different among the groups analyzing p-value < 0.001. Fisher's exact test showed that there was significant difference in the percentage of cellular steatosis among groups. **Conclusion:** It was found that cornsilk extract can be recommended as a hepatoprotective agent against DOX-induced hepatic damage.

Key words: ALT, AST, Albino Rats, Cornsilk, Cellular Steatosis, Doxorubicin, Liver.

INTRODUCTION

Cancer has been a foremost cause of morbidity and mortality globally since last many decades.[1] The management of different types of cancer varies across organ involved, its type, stage and history of the patient.[2]

Different types of anticancer drugs are used like alkylating agents, plant alkaloids, anti-metabolites, antibiotics and hormones.[3] Doxorubicin is an anthracycline antibiotic with anticancer property and is isolated from the bacterium Streptomyces Peucetius.[4] The trade name of doxorubicin is Adriamycin and Rubex and is available in Pakistan by trade names Rubicin, Doxobin, Adrim, Doxorubicin and Doxocin in the form of injections in the dose of 10mg, 20mg and 50mg. Doxorubicin can be used all alone or in combination with other anticancer drugs in order to treat different types of cancers.[5,6]

The median lethal dose (LD50) of doxorubicin is given as 56.875mg/kg per body weight.[7] The primary mechanism of action of doxorubicin involves the drug's ability to intercalate within DNA base pairs, causing breakage of DNA strands and inhibition of both DNA and RNA synthesis. Doxorubicin inhibits the enzyme topoisomerase II, causing DNA damage and induction of apoptosis. When combined with iron, doxorubicin also causes free radical-mediated oxidative damage to DNA, further limiting DNA synthesis.[8] As a consequence, can lead to lipid peroxidation as well as damage to cellular membrane, mutation of DNA , genetic changes , oxidative trauma which initiates the pathway of cell death or apoptosis.[9] Doxorubicin is seen to effect the histology of various organs like liver, pancreas, kidneys, heart, testis and stomach.[10,11] One of the most discussed and investigated side effects of DOX administration is myocardial toxicity. Toxic effect on liver by doxorubicin is also exhibited as significant raise in liver function enzymes like aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and decrease in total serum protein as well as albumin levels.[12]

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There are many nutritional supplements which are commonly used by cancer patients who think of them as anticancer and antitoxicity agents. Nutritional supplements are customized to an individual's diet, age, genetics, tumor histopathology, and treatment plans in the benefits of patients.[13] Corn silk also known as Zea mays, Stigmata maydis, Maidis stigmata and Corn Stigma. Fresh corn silk is soft, golden to yellow silk like threads that arises from the stigma of the female flower of maize which are 10 to 20 cm in length and are slightly sweetish in taste.[14] It contains carbohydrates, vitamins (C, E and K), proteins, minerals (Potassium, Calcium, Magnesium and sodium salts), volatile oils, alkaloids, tannins, saponins, steroids like stigma sterol. It contains large amount of maysin, a flavonoid.[15]

Corn silk (CS). is used as an oral anti-diabetic agent, anti-fungal, as a herbal tea, diuretic and uricosuric. CS is used worldwide to treat urinary tract infections, cystitis, gout, nephritis and prostatitis, gonorrhea, benign prostatic hyperplasia, hypertension as well as obesity.[16] Corn silk extract has protective effect on hepatic tissue which is due to decreased lipid peroxidation.[17] There are some side effects of CS that should be considered, although they are rare. If someone have low or high blood pressure or abnormal potassium levels, corn silk extract could exacerbate these issues, due to its diuretic effect. It can negatively interact with other prescription medications, as it can induce urination and eliminate the medication too rapidly.[18]

Liver is one of the most important and the second largest organ of the human body. The important functions of the liver includes protein synthesis, storage of metabolites, metabolism of fats, carbohydrates and hormones, detoxification of many drugs and excretion of bilirubin.[19] Human liver is divided into seven segments and has four lobes; right, left, caudate and quadrate lobe. Hepatic lobes of rats are comparable to human because they have same portal and hepatic vascular system.[20]

MATERIAL & METHODS

An experimental animal study was conducted at Animal house and Histology laboratory of Postgraduate Medical Institute (PGMI) Lahore. The study protocols were accepted by Advanced Studies and Research Board of University of Health Sciences (UHS), Lahore, and Ethical Committee of PGMI, Lahore. UHS/Education/126-19/1761 (14-05-2022). The Study was conducted on 30 adult albino Wistar rats of both male and female gender (Pregnant rats are excluded). A convenient sample of 30 albino rats weighing 180 - 220gm were selected was obtained from Veterinary Research Institute, Lahore.

A sample size of 30 albino rats was divided into 3 groups, a sample size of 10 rats were taken in each group (total groups = 3). First group is Control named as Group A while 2nd one is Group B and 3rd one is named as group C. group B and C are experimental group. Group A was given standard Rat feed and distilled water intraperitoneally in the dose of 1.2mg/kg/b.wt twice a week for 21 days. Group B was given Doxorubicin intraperitoneally in the dose of 1.2mg/kg /b.wt, every 4th day, twice a week for 21 days while group C was given Doxorubicin intraperitoneally and through oral lavage at the dose of 1.2mg/kg/b.wt twice a week for 21 days and corn silk extract 400mg/kg/b.wt, through oral gavage method for 21 consecutive days. Rats of all the groups were sacrificed on 22nd day, 24 hours after the administration of last Dose.

The rat was immediately euthanized after the blood sample was withdrawn through cardiac puncture. All rats were sacrificed after completion of 21 days on 22nd day 24 hours after administration of last dose. Liver was dissected out for its detail morphological and histological observations. One tissue block from each lobe was taken. The samples obtained needed to be fixed immediately in 10% neutral buffered formalin (NBF). Longitudinal sections of 3-5 micrometer thickness were obtained. Slides were stained with different stains like hematoxylin and eosin (H&E) and PAS staining. Masson's trichome stain was used to determine cellular steatosis. The parameters cellular steatosis (Cellular steatosis

0= none; 1< 33%; 2= 33-66%; 3> 66%), ALT levels and AST levels were recorded for each group rats.[21] Data was entered and was analyzed using SPSS 20.0. Frequency and Percentages were find out for qualitative variables like Cellular steatosis, while Mean ± SD was found out for quantitative variables like ALT and AST levels). Fisher's exact test was applied in order to observe the association of categorical variables with the groups. A p-value ≤ 0.05 was considered as statistically significant.

RESULTS

Fisher's exact test showed that there was significant difference in the percentage of cellular steatosis among groups. No cellular steatosis was observed in 9 (90%) rats of group A and 7 (70%) rats of group C. However in group B, cellular steatosis was observed in all rats.

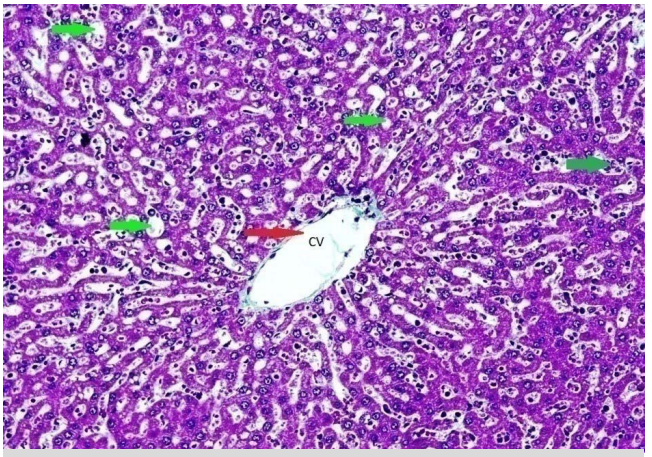

Figure-1. Photomicrograph of an liver from Experimental group (B) showing central vein (red arrow), Sinusoidal spaces (green arrow) and cellular steatosis (parrot green arrow). Masson's trichrome stain X.20

SERUM ALT and SERUM AST mg/dl

One way ANOVA test revealed that the mean ALT level and AST levels were significantly different among the groups having p-value < 0.001.

For multiple comparisons, post hoc Tukey test was used which showed that serum ALT level and serum AST in group B and C was significantly higher in comparison to group A. However, significant difference was also found in serum ALT and serum AST level between group B and C

DISCUSSION

This study presented that there was significant difference in percentage of cellular steatosis among groups. In group B, cellular steatosis was observed in all rats. Similar findings were observed in studies conducted by;[22,23,24] Results were commensurate with study conducted to exhibit the hepatoprotective and nephroprotective effect of carvedilol alone and when coadministered with diltiazem and prednisolone on doxorubicin and 5□fluorouracil□induced hepatotoxicity and nephrotoxicity in rats[25] The cause of hepatotoxicity may be increase in the malondialdehyde levels, which is a lipid peroxidation marker and causes depletion of the antioxidant enzyme, superoxide dismutase as given in studies.[26] Experiment evidently indicate that fatty liver is proficient in synthesizing less ATP than normal liver during the early phase of reperfusion following ischemia in turn causing hepatotoxicity as shown in group B whereas hepatoprotective role of CS due to its effect on cholesterol metabolism prevents steatosis as shown in group C.[27]

Cellular Steatosis	Group A n (%)	Group B n (%)	Group C n (%)	P-Value
None	9 (90.0%)	0 (0.0%)	7(70.0%)	< 0.001*
< 33%	1 (10.0%)	0 (0.0%)	3(30.0%)	
33 – 66%	0 (0.0%)	7 (70.0%)	0 (0.0%)	
>66%	0 (0.0%)	3 (30.0%)	0 (0.0%)	

Table-I. Distribution of cellular steatosis among groups

Parameters	Group A	Group B	Group C	P-Value
Serum ALT mg/dl	30.3 ± 2.8	78.3 ± 14.4	63.9 ± 16.6	< 0.001*
Serum AST mg/dl	45.1 ± 8.3	147.8 ± 23.0	113.8 ± 17.8	< 0.001*

Table-II. Comparison of Serum ALT mg/dl and Serum AST mg/dl among groups:

Mean ALT levels were significantly different statistically among all three groups (p-value < 0.001) and serum ALT level in group B and C was significantly higher as compared to group A. However, significant difference was also found in serum ALT level between group B and C. It was also concluded that the mean AST were also significantly different among the groups (p-value < 0.001) and showed that serum AST level in group B and C was significantly higher as compared to group A. However, significant difference was also found in serum AST level between group B and C. Results were in agreement with study done by treating rats with doxorubicin which concluded a significant (P < 0 .05) increase in the levels of serum AST, ALT, and ALP.[23,26]

In comparison, a study was conducted by Mustafa et al. (2015) which showed deteriorating liver function in the DOX treated group, which was represented by the significant raise in levels of serum ALT, serum AST and total bilirubin in comparison to the control. Contradictory results were given by a study which showed that AST activity was significantly reduced in the group which is in tandem exposed to a higher dose of doxorubicin and resveratrol while serum ALT activity was raised in animals exposed to both resveratrol and doxorubicin in lower dose but it is decreased among the rats treated with resveratrol and a high dose of the doxorubicin.[28]

CONCLUSION

From the foregoing results, it is clear that CS can protect the liver against hepatotoxicity induced by DOX. These changes can be ameliorated with the use of corn silk extract as being antioxidant it has maintained hepatic tissue architecture and significantly reduced degeneration of hepatocytes and liver parenchyma by counter-balancing DOX induced oxidative stress. Thus corn silk extract can be recommended as a hepatoprotective agent against DOX-induced hepatic damage due to their easy, rapid and safe dietary administration, especially with increasing incidence of cancer and use of anticancer drugs like DOX. Based on these findings, the present study will produce an awareness of side effects of anticancer drugs and promote use of natural supplements like corn silk extract.

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3	Saba Tahir	Proof reading.	
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