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Research Article

PROTECTIVE EFFECT OF TAURINE ON HISTOPATHOLOGICAL CHANGES DUE TO PROPANIL TOXICITY

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ABSTRACT

The present study was designed to investigate the detrimental effects of propanil on liver and kidney of mice and probable alleviating capability of silymarine against such intoxication effects. Methods: In an experimental study 36 albino mice were distributed in six equal groups of six each as follows: Control group, 100mg propanil/kg, 100mg taurine/kg, 200mg taurine/kg, propanil (100 mg/kg) + taurine (100 mg/kg), propanil (100mg/kg) + taurine200mg/kg. Treatment was via oral route and was fed once daily for 90 days. Propanil revealed marked degenerative and necrotic alterations in kidney and liver. Taurine improved propanil induced histopathological alteration.

INTRODUCTION

Rice, potato is very commonly and extensively grown crops, and often dominate the most part of landscape and thereby it changes the ecological system in many ways. Modern cultivation is dependent on agrochemicals as pesticides, insecticides mainly herbicides. Herbicides are quite an important class of agricultural pesticides. Propanil (3 ,4 dichloropropionanilide) is an acetanilide which is used to control broadleaf weeds and most extensively used as post emergent herbicides for rice, wheat and potato production worldwide. Propanil is among top twenty pesticides used in agriculture (*1*).

As propanil is widely used on crops like wheat and rice which we use on daily basis that suggests that human could be at risk of high level exposure. World Health Organization (*2*) has considered Propanil slightly hazardous in terms of human risk. (3).

According to one study propanil can alter histopathology of liver and kidney by changing dose of it in tissue of exposed mice (4*).*The scope of occupational exposure to the people who are dealing with this chemical like retailers of product, farmers, and people in manufacturing units is also there. Chloracne observed in industrial workers during propanil manufacturing which was primarily due to other chemical contaminants present in it (5), (6).

Study has also conducted on mammalian toxicity as in mice; it suppresses the activity of natural killer cells which suggests that it has immunotoxic potential (7), (18), (9). When given intraperitoneally to mice, it hinders the function of nervous system and many reflex activities (*10).* Male rats were fed 1600 mg kg propanil over a period of 2-years and mortality was observed in them (11). Hemo-lytic anemia and methemoglobinemia, is found primarily in self poisoned humans who ultimately led to their death (6), (12). Propanil is an immunotoxicant in many models, which reduces the formation of cytokines as well as the number of CD41CD81 thymocytes (9), (13), (14), (15). In cases of human propanil poisoning nephrotoxicity and hepatotoxicity have been reported (16), (12) and animal studies (17), (18).

Antioxidants play important role in regulation of physiological and pathological processes. Antioxidant protect the cells and tissues against deleterious effects of reactive oxygen species and other free radicals. Taurine (2-aminoethanesulphonic acid) is actually an amino acid which is present in many animal tissues like kidney, liver and brain majorly but in very minute

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quantity. (19*)*. Taurine is synthesized during cysteine and methionine metabolism. Taurine function actively in osmoregulation, detoxification, membrane stabilization etc. *(20),(21).* Taurine acts as antioxidant because it can stabilize the bio-membranes and scavenge reactive oxygen species *(19).* It has been seen in urine excretion patterns many a times that taurine participates in many physiological and biological processes in kidney. As taurine participates in several biological processes in kidney, and kidney affects taurine homeostasis. As taurine is soluble in waters and it doesn't incorporate into protein structure, so it act as zwitterions at physiologic pH and maintain osmotic balance within cell an it is present in very minute quantity inside it *(20), (21).*

To the best of our knowledge, there are no studies concerning the nephroprotective effect of taurine against propanil intoxication. Therefore, the present study was carried out to investigate (a) the adverse effect of subchronic propanil intoxication on the kidney based on serum biochemical parameters, oxidative stress (b) the probable ameliorating effect of taurine against propanil intoxication in mice.

METHODOLOGY

Chemicals

Herbicide propanil PESTANAL #, analytical standard was purchased from Sigma-Aldrich Co.Ltd.St. Louis, USA and taurine was purchased from LOBA chemie, (EDTA) hydrogen peroxide, sulphuric acid, diethyl triamine penta acetic acid, sodium dodecyl sulphate, TBA and pyrogallol, were purchased from E Merks Ltd. Mumbai India. All other chemicals were of technical grade and purchased from Loba Chemie, Mumbai India.

Animals

Colony bred Swiss albino mice weighing 18-20gm obtained from Institute of Animal health and Veterinary and Biological Products, Rasalpura, Mhow, Madhya Pradesh were used for this study. The animals were maintained at 22±3^{o}C with 50-70% relative humidity and 12:12 hrs of light and dark cycles and were kept in well ventilated cages. The animals were fed with calculated amount of laboratory pellet diet procured from government agricultural college, Indore, India, and water *ad libitum*. Animals were maintained as per the guidelines laid down by (CPCSEA) Ref.No- 1063/DDS/2014-15.

Experimental protocol

Mice were divided into six groups of six animals in each group and were allowed free access to feed and water for 20 days before the commencement of the experiment. As both the drugs were given in pellet diet, so mice were closely studied for a period of 20 days to evaluate the consumption of food according to already studied equation. Daily dose was calculated on the basis of following equation: DD = (SD X BW) / F1 (Research Diet)

DD=diet dose (mg cmpd/kg Diet), SD= Single Daily Dose (mg cmpd /kg BW/day) BW= Body Weight (gm BW/animal), F1= Daily Food Intake (gm Diet/day) and the group were as follows;

Group 1- Control animals (no treatment)
Group 2- Propanil treatment)
Group 3 - Taurine treatment (100mg/kg BW)
Group 4-Taurine treatment (200mg/kg/body weight a double dose treatment)
Group 5- Propanil (100mg/kgBW) + Taurine(100mg/kg BW)
Group 6-propanil (100mg/kg BW) + Taurine (200mg/kg BW)

The dose of nephro-protectant drug was increased as it was observed that the protection was improved by increasing the dose to twice. All the above groups except group 1 were treated daily for the period of 90 days.

RESULT

In order to evaluate the effects of Propanil on mouse kidney, we treated mice for 90 days and euthanized them after administration of the final dose. There was not any significant clinical sign of disease during the experimental period and at the end of the assay, all the animals were still alive.

Animal's water and food consumption

There was statistically significant difference in water consumption during the experimental period, although throughout the experiment, the Propanil-treated group manifested lower water consumption compared to the control group (data not shown). Food intake was also lower in the propanil-treated group, however, only at the 9th week this became statistically evident (p=0.045) compared to the control group. The mean weight of the animals' organs was taken.

Tissue and Homogenate Preparation: At the end of 12 h, after overnight fasting, mice were sacrificed by cervical dislocation; tissues were quickly removed and rinsed with ice- cold saline, buffer.

Histological evaluation: Representative fragments of each organ were fixed in 10% buffered formalin for 24-48 hrs further these tissues were processed by routine method of dehydration in graded alcohol, clearing in xylene and than embedded in paraffin wax. Tissue sections of 2 µm were processed and stained with haematoxylin and eosin (H&E) *(22).* The livers were sectioned for reticulin and Masson's trichrome staining, according to the techniques described by Jones. Liver samples were analyzed via optical microscopy to identify lesions. The following parameters were evaluated architecture, fibrosis, bile ductal hyperplasia, cholestasis, hepatocyte necrosis, the presence of inflammatory cells, hydropic degeneration, hyperplasia, anisokaryosis, binucleated cells, pseudo-nucleoli, apoptosis, focal hepatic necrosis and mitosis.

Macroscopic and microscopic evaluation: Macroscopic changes were not identified on the organs collected from the control group; liver from one mouse of the propanil treated group exhibited a whitish-colored lesion with a diameter less than 1 mm. The histo-pathological liver lesions discovered were confined to only propanil exposed group No histological changes were found in the livers of mice belonging to the control group. Both groups preserved normal liver architecture (Figure 1A).

Liver

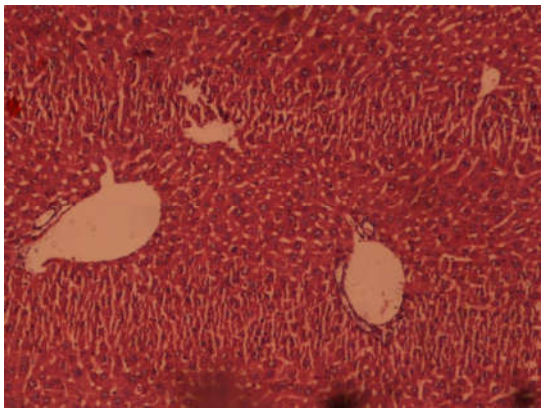
Normal liver tissue showed the typical architecture with a central vein and hepatocytes radiating from it (Fig.1) Livers from animals exposed to propanil presented fatty changes

cytoplasmic hydropic degeneration and hemorrhages in group 2; and focal hepatic necrosis (Figure 2). In group 2 showed fatty and hydropic changes with congestion of sinusoids and infiltration of inflammatory cells treatment with taurine 100 mg/kg dose partially protected the hepatocytes, with liver tissues showing mild focal necrosis with fatty changes (Figure 5a-d). When the dose was doubled (200 mg/kg), there was complete restoration of hepatic architecture without any degenerative changes in taurine along with propanil. Treatment with taurine at 100 mg/kg dose partially protected the hepatocytes with liver tissues showing mild focal necrosis with fatty changes. This indicates there was not only functional improvement, but also structural normalization of liver parenchyma with treatment with administration of taurine. When the dose of taurine was doubled (200 mg/kg), there was significant restoration of hepatic architecture without any degenerative changes. The absence of inflammatory cells may be a possible indicator of the anti-inflammatory action of taurine. However, some of the sections even at 100 mg/kg dose showed mild fatty changes. Hence treatment with taurine ameliorated the harmful effect of propanil and mice liver exhibited normal histological structure except few vacuolations.

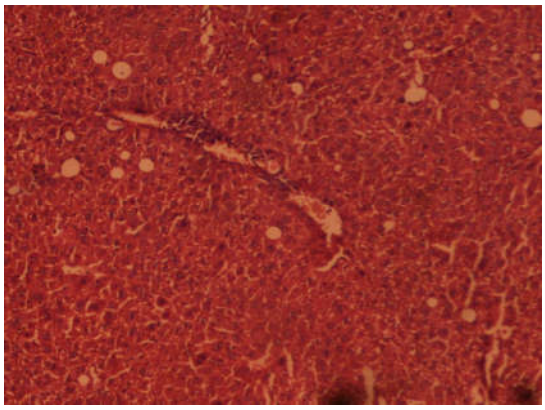
Kidneys: Out of 6 mice sacrificed on 90th day, kidney of 2 mice shown focal area of necrosis while no significant lesions were seen in other groups. In the control group of mice showed normal morphology of the renal parenchymal cell with well defined normal glomeruli and tubules as shown in fig as compared to control group kidney of treated mice which exhibited acute necrosis of tubular epithelial layer, mainly in cortical region and at junction of medulla and cortex. Bowman capsule were dilated as compared to control, and there were evident atrophy found in glomerular cells along with prominent degenerative changes. There were circulatory disturbances like congestion at many places in intertubular blood vessels and edema in interstitial cells and opposite to that the group treated with silymarine along with toxicant, silymarine improved the intensity of lesions. There was only mild congestion of intertubular blood vessels in taurine with propanil group but on whole treatment with taurine exhibited nearly normal structure of renal tissues.

DISCUSSION

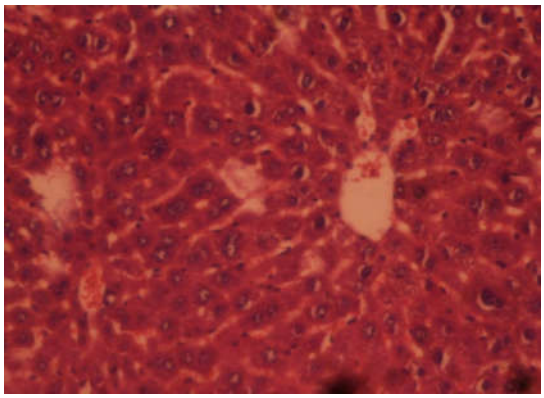
The studies in rats and mice showed toxic effect of any toxicant not only on blood or developmental processes but also on the non reproductive organs like kidney and liver (25). The effect of propanil on kidney could be attributed to lipid peroxidation of cell membrane which generated such species that lead to cells protein destruction and their by promoted cell degradation. Propanils effect on liver tissue may be because, as liver acts as reservoir structure and primary site of aryl acyl amidase hydrolysis and further oxidation reactions. Propanil acted as hepatotoxicant as, it damaged the liver cells mainly by inducing oxidative damage and lipid peroxidation. Such results were reported earlier also (26), where it was clearly shown that propanil caused histopathological alteration in liver and kidney tissue and (25),(26),(27). They found that propanil treated rats shown hepatocellular necrosis, infiltrated lymphocytes, and many areas of necrosis (28), (29).



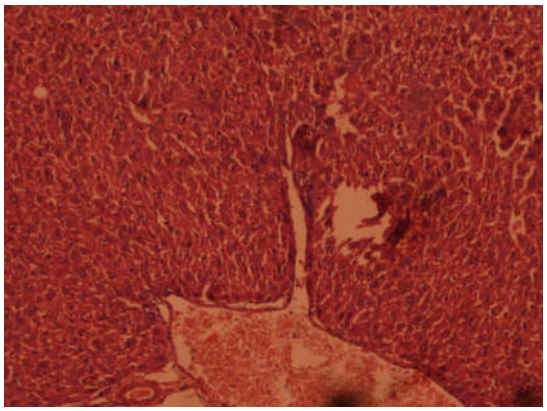
Section of of liver of group 1 at 90th day showing normal architecture



Section of liver of group 2 at 90th day post treatment showing congested blood vessel and vacculation

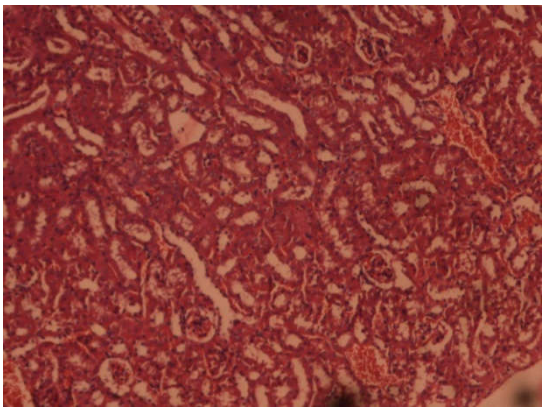


Section of liver of group 2 at 90th day showing necrosis and vacuolation (H&E 20X)

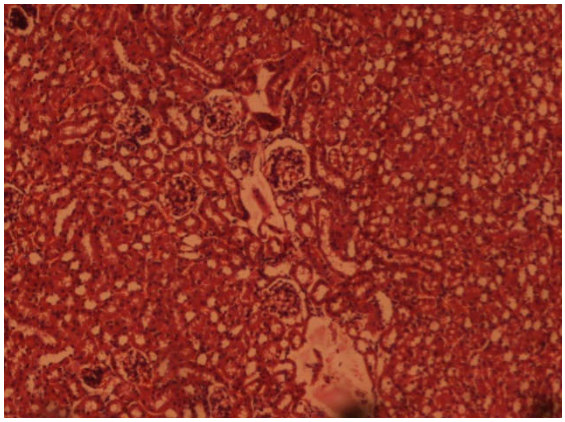


Section of liver of group 2 at 90th day post treatment showing vacuolation and dilated sinusoidal places along with hemmorages.

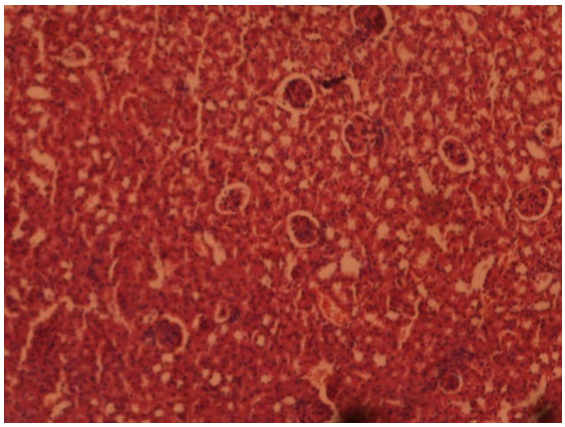
When we gave taurine along with propanil, it leads to not only functional improvement but also structural restoration and normalization of liver parenchyma.



Section of kidney of group T1 at 90th day post treatment showing necrosis and extensive tubular degeneration (H&E 10X)



Section of kidney of group 5 at 90th day post treatment showing mild degenerative changes



Section of kidney of group 6 at 90th day post treatment showing almost normal architecture

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