

Influence of *Eclipta alba* on serum alanine aminotransferase and aspartate aminotransferase activity in rabbits

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Received: 11 May 2018

Revised: 26 May 2018

Accepted: 04 June 2018

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ABSTRACT

Background: Paracetamol is a recognized antipyretic, analgesic drug which produces hepatic necrosis in high doses. *Eclipta alba* elaborates a vast array of biologically active compounds that are chemically diverse and structurally complex.

Methods: Randomized open controlled experimental study Estimated levels of Serum aspartate aminotransferase (AST), Serum alanine aminotransferase (ALT) and Hepatoprotective action of in High doses of Paracetamol on serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity.

Results: ALT in all the groups including Control group (A) was (51.8±4.56IU/L). Paracetamol treated group (B) the ALT level increased at 48 hours and continued to be high up to 60 days (136.4±20.73IU/L) then decreased to (113.7±11.35IU/L) at 90 days. AST in all the groups including Control group (A) was (22.5±1.23IU/L). Appropriate antioxidant in appropriate doses as a matter of routine whenever hepatotoxic or potentially hepatotoxic drugs are prescribed. In Paracetamol treated group (B) the AST level increased at 48 hours and continued to be high up to 60 days (99.4±9.73IU/L) then decreased to (85.4±7.39IU/L) at 90 days.

Conclusions: Appropriate antioxidant in appropriate doses as a matter of routine whenever hepatotoxic or potentially hepatotoxic drugs are prescribed.

Keywords: Alanine aminotransferase, *Eclipta alba*, Paracetamol

INTRODUCTION

The involvement of free radicals in the pathogenesis of liver injury has been investigated for many years in a well-defined experimental system. Studies conducted to find out the role of oxidative stress in alcohol induced cirrhosis. These studies have shown increased lipid peroxidation by HO radical and hydroperoxides in experimental acute and chronic alcoholic liver diseases. It has been suggested that ROS and lipid peroxidation may play a role in pathogenesis of hepatic fibrosis with loss of normal liver

architecture. In another study it is found that plasma levels of vitamins are low in patients with chronic cholestatic liver diseases.¹

Paracetamol is a recognized antipyretic, analgesic drug which produces hepatic necrosis in high doses. The drug is excreted as sulfate and glucuronide conjugate. After administration of toxic doses of Paracetamol, the Sulfataion and glucuronidation routes become saturated and hence, higher percentages of Paracetamol molecules were oxidized to highly reactive N-acetyl-p-benzoquinone imine by cytochrome P-450 enzymes. The Semiquinone

radicals, obtained by one electron reduction of N-acetyl-p-benzoquinone imine, can covalently bind to macromolecules of cellular membrane which increases the lipid peroxidation resulting in the tissue damage. Higher doses of Paracetamol and N-acetyl-p-benzoquinone imine, alkylate, oxidize intracellular GSH, results in the depletion of liver GSH pool subsequently leads to increased lipid peroxidation thereby causes liver damage.²

Liver diseases are caused by toxic chemicals, excessive consumption of alcohol, infections and autoimmune disorders. Presently drug-induced liver toxicity is a common cause of liver injury.³

In spite of the tremendous advances made in modern medicine, fully satisfactory effective hepatoprotective medicine is not available. Numerous plants and polyherbal formulations are claimed to possess hepatoprotective activities, but the management of liver disease is still a challenge to have the health care professionals.

Eclipta alba belongs to Asteraceae family and very common in tropical and subtropical regions. The plant grows abundantly as a weed in moist places all parts of Thailand. The herb has been used in traditional medicine of Asia, that's especially in India and China. It grows commonly in moist places as a weed all over the world. Main active principles consist of coumestans like Wedelolactone, Desmethylwedelolactone, Furanocoumarins, eclalbatin. Oleanane and Taraxastane Glycosides. It is also used in skin diseases.

The alcoholic extract of the plant has shown antiviral activity against Ranikhet disease virus. The plant is commonly used in hair oil all over India for healthy black and long hair.

The fresh juice of leaves is used for increasing appetite, improving digestion, and as a mild bowel regulator. It is also used in viral hepatitis to promote bile flow and to protect the Parenchyma. It is popularly as an enhancer memory and learning. The plant has a reputation as an anti ageing agent in Ayurveda. It is used as a general tonic for debility. Externally it is used for inflammation. Minor cuts and burns and the fresh leaf-juice is considered very effective in stopping bleeding. Leaf juice mixed with honey is also used for children with upper respiratory infections and also used in eye and ear infections. It is a source of coumestans-type compounds used in Phytopharmaceutical formulations of medicines prescribed for treatment of cirrhosis of the liver and infectious hepatitis.⁴

Aim and objectives

Estimate levels of Serum aspartate aminotransferase (AST), Serum alanine aminotransferase (ALT). Hepatoprotective action of *Eclipta alba* in High doses of Paracetamol on serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity.

METHODS

Locus of study

The present study was undertaken in Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha. All the Biochemical procedures were carried out in Central Research Laboratory, DMIMS, Sawangi (M), Wardha.

The data was collected from July 2007 to February 2010.

It was randomized open controlled experimental study. Pilot study was conducted to determine the sample size. Accordingly, 120 Rabbits were selected.

The approval of Institutional Animal Ethical Committee was obtained vide their letter no. DMIMS (DU)/IAEC/2006-07/1413, dated 23/02/2007.

Paracetamol induced acute hepatotoxicity. Dose of Paracetamol was 98mg/kg. Route of drug administration was oral. Collection of blood sample was day 0, day 2, day 15, day 30, day 45, day 60, day 75, and day 90.

Eclipta alba aqueous leaf extract. These drugs were procured from Department of Dravyaguna, MGACH and RC, Salod (H), Wardha. The experts of Department of Dravyaguna, MGACH and RC authentication of the dried leaf and fine powder was done in Ayurvedic Pharmacy Laboratory. Solvent used: distilled water.

Method of preparation of Eclipta alba aqueous leaf extract

One kg of freshly collected, shade dried, powdered leaves of *a. indica* were ground in four liters of distilled water and allowed to soak overnight. The suspension was centrifuged at 5000 rpm for 20 min and filtered through a Whatman N0 -1 filter paper. The supernatant fluid was allowed to evaporate in glass Petri dishes under tube light to provide heat and to prevent dampness so that no organism growth occurs. When completed dry the powder was collected by scraping and was stored. Stock solution of aqueous extract was prepared by dissolving 100mg/ml solution in distilled water.^{5,6}

Collection and preparation of blood sample

Requirements include animals, cotton, 26G needle, 95% v/v alcohol, o-Xylene, surgical blade and blood sample collection tube. The animal was placed in a restrainer. Ear was cleaned with 95% v/v alcohol and local anesthetic cream was applied on the collection site 10 min prior to sampling. (If required, the o-Xylene/topical vasodilator applied topically on the collection site to dilate blood vessels). Size 11 surgical blade was used to cut the marginal ear vein and blood was collected in a collecting tube. A 26G needle was used to collect blood from animal marginal vein. After collecting blood, clean sterile cotton

is kept on the collection site and finger pressure is applied to stop the bleeding.⁷

RESULTS

ALT levels, as shown in Table 1.

ALT in all the groups including Control group (A) was (51.8±4.56). In Paracetamol treated group (B) the ALT level increased at 48 hours and continued to be high up to

60 days (136.4±20.73IU/L) then decreased to (113.7±11.35IU/L) at 90 days but remained high with respect to untreated control. This difference was found to be statistically significant (P<0.001). Drug was administered as single dose once daily for seven days (group C₃), ALT levels started decreasing after 48 hours (88.7±8.52IU/L) and came back to control after 60 days (52.5±6.88IU/L). (group D₃), ALT levels started decreasing after 48 hours (89.3±9.23IU/L) but took 90 days to return to the control values (51.1±6.45IU/L).

Table 1: *Eclipta alba* on ALT.

Groups ↓	Time interval →							
	Day 0	Day 2	day 15	day 30	day 45	day 60	day 75	day 90
A	51.8±4.56	52.4±5.19	51.8±5.37	50.9±4.32	51.7±4.47	52.7±5.79	52.5±4.87	51.8±5.65
B	51.7±5.43	98.5±7.23	112.7±9.32	118.4±10.59	127.2±12.56	136.4±20.73	123.8±17.12	113.7±11.35
C ₃	51.4±5.83**	88.7±8.52**	74.6±7.75**	67.9±6.47**	61.5±6.54**	52.5±6.88**	52.4±7.12**	51.1±5.96**
D ₃	52.8±5.25	89.3±9.23	86.4±9.45	79.8±8.55	70.4±7.38	64.2±6.94	52.9±6.35	51.1±6.45

A= Control no drug.

B= Paracetamol alone.

C₃= Paracetamol+ *Eclipta alba* immediate and daily for 7 days.

D₃= Paracetamol+ *Eclipta alba* single dose immediately after Paracetamol administration.

**P<0.001 in comparison with Paracetamol control.

Table 2: *Eclipta alba* on AST.

Groups ↓	Time interval →							
	Day 0	Day 2	day 15	day 30	day 45	day 60	day 75	day 90
A	22.5±1.23	21.3±1.98	22.8±1.43	20.8±1.37	21.7±1.34	20.9±1.69	21.1±1.45	22.7±1.56
B	20.7±1.43	51.5±5.23	66.7±7.32	77.4±8.59	87.2±8.56	99.4±9.73	87.8±8.99	85.4±7.39
C ₃	20.1±1.23**	48.6±3.29**	40.2±3.77**	34.9±2.35**	28.5±1.22**	22.7±1.28**	22.8±1.23**	22.5±1.73**
D ₃	20.1±1.44	50.4±4.16	47.8±6.47	43.7±6.78	37.5±4.64	33.9±2.11	28.4±1.35	22.3±1.93

A= Control no drug.

B= Paracetamol alone.

C₃= Paracetamol+ *Eclipta alba* immediate and daily for 7 days.

D₃= Paracetamol+ *Eclipta alba* single dose immediately after Paracetamol administration.

**P<0.001 in comparison with Paracetamol control.

AST levels, as shown in Table 2.

AST in all the groups including Control group (A) was (22.5±1.23IU/L). In Paracetamol treated group (B) the AST level increased at 48 hours and continued to be high up to 60 days (99.4±9.73IU/L) then decreased to (85.4±7.39IU/L) at 90 days but remained high with respect to untreated control. This difference was found to be statistically significant (P<0.001).

In *Eclipta alba* treated group wherein the drug was administered as single dose once daily for seven days (group C₃), AST levels started decreasing after 48 hours (48.6±3.29IU/L) and came back to control after 60 days (22.7±1.28IU/L).

However, group D₃, AST levels started rising after 48 hours (50.4±4.16IU/L) and came back to control after 90 days (22.3±1.93IU/L).

DISCUSSION

In this study, we observed that at the point of commencement of study, the overall mean value, of ALT in all the groups including Control group (A) was (51.8±4.56).

In Paracetamol treated group (B) the ALT level increased at 48 hours and continued to be high up to 60 days (136.4±20.73IU/L) then decreased to (113.7±11.35IU/L) at 90 days but remained high with respect to untreated control. This difference was found to be statistically significant (P<0.001).

In *Eclipta alba* treated group wherein the drug was administered as single dose once daily for seven days (group C₃), ALT levels started decreasing after 48 hours (88.7±8.52IU/L) and came back to control after 60 days (52.5±6.88IU/L).

Whereas in *Eclipta alba* treated group, wherein the drug was administered immediately as a single dose (group D₃), ALT levels started decreasing after 48 hours (89.3±9.23IU/L) but took 90 days to return to the control values (51.1±6.45IU/L).

Result observations were reported by Tabassum and Agrawal, Saxena et al, and V. K. Lal et al, evaluated *Eclipta alba* as hepatoprotective drug.

In this study, we observed that at the point of commencement of study, the overall mean value, of AST in all the groups including Control group (A) was (22.5±1.23IU/L).

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This study findings are in resemblance to those of Tabassum and Agrawal Saxena, et al, V. K. Lal et al, evaluated *Eclipta alba* as hepatoprotective drug.⁸⁻¹⁰

CONCLUSION

In the view of the above it is prudent to prescribe appropriate antioxidant in appropriate doses as a matter of routine whenever hepatotoxic or potentially hepatotoxic drugs are prescribed. And also, as a preventive measure everyone should take diet rich in antioxidants.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Animal Ethics Committee (DMIMS (DU)/IAEC/2006-07/1413)

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Cite this article as: Kale BP, Rauf MJ. Influence of *Eclipta alba* on serum alanine aminotransferase and aspartate aminotransferase activity in rabbits. Int J Basic Clin Pharmacol 2018;7:1243-6.