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RESEARCH ARTICLE

Hepatoprotective Effect of *Terminalia Chebula* on Gentamicin Induced Toxicity in Rats

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ABSTRACT

A study was carried out to analyze the hepatotoxicity induced by administration of gentamicin by analyzing liver specific parameters like alanine amino transferase, aspartate amino transferase, superoxide dismutase, blood urea nitrogen and creatinine in rats and to confirm the same by histopathological examination. An attempt was also made to study the possible hepatoprotective effect of *Terminalia chebula* on gentamicin induced toxicity and compare the same with that of silymarin. The results of this study showed that gentamicin administered at a dosage of 80 mg/kg b.wt. i/p once daily for seven days produced significant elevation of serum biochemical parameters like ALT, AST with significant reduction in the level of total protein and albumin. Administration of aqueous extract of *Terminalia chebula* significantly restored these parameters. The results of the present study have suggested that *Terminalia chebula* plant extracts can be used as a protective agent in gentamicin induced hepatotoxicity.

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INTRODUCTION

Gentamicin, an aminoglycoside is one of the most widely used antibiotics in veterinary practice. The clinical use of aminoglycosides may be limited by the development of toxic side effects such as hepatotoxicity, nephrotoxicity, ototoxicity, etc. To maintain the clinical utility of this important group of compounds, various authors have attempted co-treatment with some plant extracts which might ameliorate gentamicin induced toxicity. In the present study we have focused on the alleviatory effect of *Terminalia chebula* on the hepatic damage induced by gentamicin. Parameters like ALT, AST, total protein, and albumin were monitored to study the liver damage and to understand the possible protective effects of *Terminalia chebula*.

MATERIALS AND METHODS

Inbred male albino rats of Wistar strain weighing 120-150 g were obtained from Laboratory Animal Medicine, Tamil Nadu Veterinary and Animal Sciences University, Madhavaram Milk Colony, Chennai – 600 051, Tamil Nadu, India. They were housed in cages , acclimatized to the standard laboratory conditions and were fed with standard dry pellet feed and provided drinking water *ad libitum.*

Terminalia chebula (aqueous extract) obtained from M/s Natural Remedies, Bangalore, India, silymarin obtained from M/s Microlabs, Goa, India and gentamicin sulphate procured from M/s Intas Pharmaceuticals, Matoda, Gujarat, India *as gratis* were used in the study. All other chemical reagents used were of analytical grade.

Thirty male rats were divided randomly into five groups of six in each and subjected to the following treatments.

Drug treatment was continued for seven days. At the end of the experiment, blood samples were collected from all the rats and sacrificed. Serum was separated by centrifuging at 800 g for five minutes for biochemical estimations which included alanine amino transferase (ALT), aspartate amino transferase (AST) (Reitman and Frankel, 1957), total protein (Markwell *et al*., 1978) and albumin (Gendler *et al*., 1984).

Results were analyzed by complete randomized design using SPSS software (Version 10) and comparison of the means was done by using Duncan's Post-Hoc test (multiple comparison tests).

RESULTS

Hepatoprotective activity of *Terminalia chebula* in gentamicin induced toxicity model was tested at two different dose levels *viz*., 125 and 250 mg/kg of body

Control	Negative control
Gentamicin	Gentamicin sulphate 80 mg/kg B.W. i/p
TC 125	Gentamicin sulphate 80 mg/kg B.W. i/p +*Terminalia chebula* 125 mg/kg B.W. p/o
TC 250	Gentamicin sulphate 80 mg/kg B.W. i/p +*Terminalia chebula* 250 mg/kg B.W. p/o
Silymarin	Gentamicin sulphate 80 mg/kg B.W. i/p + silymarin 50 mg/kg B.W. p/o.

Table 1: Effect of *Terminalia chebula* extract on biochemical parameters in experimentally induced gentamicin toxicity

	ALT (IU/L)	AST (IU/L)	Total Protein (g/L)	Albumin (g/L)
Control	42.33^{a}±2.03	143.30^{a}±8.20	6.86^{d}±0.27	4.86^{d}±0.14
Gentamicin	63.17^{e}±2.02	230.67^{d}±8.29	4.48^{a}±0.14	3.27^{a}±0.06
TC 125	58.25^{de}±1.49	204.68^{c}±15.99	5.85^{b}±0.1	4.21^{b}±0.05
TC250	57.04^{d}±1.23	199.49^{c}±17.66	6.11^{bc}±.08	4.51^{bcd}±0.16
Silymarin	42.82^{ab}±2.02	164.49^{b}±11.22	6.46^{c}±0.09	4.76^{cd}±0.15

Means bearing different superscripts in the same column differ significantly ($p<0.05$); All values are expressed as Mean ± S.E, n=6

weight. Serum and tissue biochemical parameters were studied to assess the hepatoprotective effect. The mean ± S.E values of ALT, AST, serum total protein and serum albumin are furnished in Table 1. The concentration of ALT in control group was observed to be 42.33 ± 2.03. Rats belonging to gentamicin group showed significantly ($P<0.05$) higher level of ALT activity (63.17 ± 2.02). *Terminalia chebula* at both the dose level significantly ($P<0.05$) reduced ALT activity but to a moderate level only. However silymarin reduced ALT activity almost towards control group (Table-1). Gentamicin group has shown significantly ($P<0.05$) higher AST activity (230.67 ± 8.29) compared to the control (143.30 ± 8.20). *Terminalia chebula* extract significantly reduced the AST activity to a moderate level. Silymarin however has produced a more significant reduction in AST activity when compared to the plant extract treated group (Table-1). There was a significant ($P<0.05$) reduction of total protein content in gentamicin group (4.48 ± 0.14) when compared with control (6.86 ± 0.27). Both the extracts were found to increase the total protein towards control. *Terminalia chebula* at high dose level was found to increase total protein significantly ($P<0.05$) which was comparable to silymarin (6.46 ± 0.09) (Table-1). There was a significant ($P<0.05$) reduction of serum albumin observed in gentamicin treated group (3.27± 0.06) when compared to normal (4.86 ± 0.14). Though the extract of *Terminalia chebula* at both dose levels had revealed significant ($P <0.05$) rise in albumin compared to gentamicin group, silymarin treated group (4.76 ± 0.15) brought the albumin to near control levels (Table-1).

DISCUSSION

One of the most sensitive and dramatic indicators of hepatocyte injury is the release of intracellular enzymes such as ALT and AST in the circulation. During hepatic damage, these transaminases present in the liver cells leak in to the serum, resulting in increased concentrations. The elevated activities of these enzymes are indicative of cellular leakage and loss of the functional integrity of the cell membranes in liver (Rajesh and Latha, 2004). The measurement of ALT is a sensitive and valuable indicator of hepatic injury since the enzyme activity is confined to the cytoplasm of liver (Loeb, 1997).

In the present study, the ALT level was significantly increased in gentamicin group when compared to control group. Garg *et al*. (1996) reported that administration of gentamicin at a dose rate of 40 mg/kg to rabbits for a period of five days increased the levels of ALT compared to control group. The increase could be attributed to gentamicin which was able to cause specific hepatic injury during the treatment period.

In *Terminalia chebula* treated group, the enzyme level showed a significant decrease. The stabilization of these enzyme levels by the crude extract of *Terminalia chebula* and the standard drug silymarin indicated the improvement of functional status of liver. Manna *et al*. (2006) reported that administration of *Terminalia arjuna* aqueous extract successfully restored the alterations of ALT level caused by CCl_4 administration.

The AST is found in sufficient concentration in liver, kidney and other tissues and considered useful to evaluate in hepatocellular injury (Turk and Casteel, 1997). In our study, gentamicin treated group showed a significant increase in the AST level when compared to control. *Terminalia chebula* treated groups produced a significant moderate reduction in AST level. However silymarin produced a higher reduction in AST level. Garg *et al*. (1996) reported that administration of gentamicin at a dose rate of 40 mg/kg to rabbits for a period of five days increased the levels of AST compared to control group.

The present study showed significant reduction of total protein in gentamicin group when compared to the control. Extracts of *Terminalia chebula* and silymarin-treated groups showed significant increase in total protein level when compared to gentamicin treated group.

There was a significant ($P<0.05$) reduction of serum albumin observed in gentamicin group (3.27 ± 0.06) compared to normal (4.86 ± 0.14). Though the extracts of *Terminalia chebula* had revealed significant ($P<0.05$) rise in albumin compared to gentamicin group, silymarin treated group (4.76 ± 0.15) brought the albumin back to near control levels.

Conclusions

Hepatoprotective effect of *Terminalia chebula* was studied in a model of gentamicin induced toxicity in rats. Gentamicin was administered intraperitoneally at the dose of 80 mg/kg body weight once daily for seven days. Significant elevation of serum biochemical parameters like ALT, AST with significant reduction in the level of total protein and albumin occurred.

Cotreatment with aqueous extract of *Terminalia chebula* significantly restored the liver specific parameters. Thus the results of the present study suggest that *Terminalia chebula* plant extracts can be used as protective agent in gentamicin induced hepatotoxicity.

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