Scholarly Research Journal for Interdisciplinary Studies,
Online ISSN 2278-8808, SJIF 2018 = 6.371, www.srjis.com
PEER REVIEWED & REFEREED JOURNAL, JAN-FEB, 2019, VOL- 6/49

PHARMACOLOGICAL EVALUATION OF PLANT-DERIVED EXTRACTS AGAINST ACETAMINOPHEN-INDUCED ACUTE HEPATIC INSULT

Dr. Anjana Jadon

Assistant Professor Zoology, Government Girls Degree College Chhibramau, U.P., India

Email- anjanajadon83@gmail.com

Abstract

Present investigation was aimed to evaluate the hepatoprotective effect of Terminalia belerica fruit extract at four different doses (100, 200, 400 and 800 mg/kg, p.o.) against acetaminophen (APAP, 2.0 g/kg, p.o. once only) induced liver injury in female albino rats. APAP administration caused significant increase in the activities of serum transaminases, alkaline phosphatase and lactate dehydrogenase ($P \leq 0.05$). Toxicant caused injury in the parenchymal cells thereby affecting triglycerides, cholesterol, total and direct bilirubin level. A significant decline was observed in total protein content, blood sugar level and glycogen content whereas level of albumin increased during toxicity. Hepatic lipid peroxidation increased significantly on the contrary significant depletion was observed in reduced glutathione level after acetaminophen administration ($P \leq 0.05$). Activities of hepatic microsomal drug metabolizing enzymes i.e. aniline hydroxylase and amidopyrine-N-demethylase were inhibited significantly after APAP intoxication. Single administration of extract after toxicant administration significantly reversed the APAP induced alterations in the liver function tests and drug metabolizing enzymes. All biochemical results indicated that 400 and 800 mg/kg dose of extract were equally effective when analyzed statistically. It was observed that acetaminophen caused significant histopathological damage (inflammation, necrosis and vacuolation) in hepatocytes. These changes were recouped with therapy of extract (400 mg/kg). Thus it may be concluded that Terminalia belerica extract possessed considerable hepatoprotective potential.

Keywords: *Acetaminophen; Terminalia belerica Roxb.; Hepatoprotection; Liver function tests; Drug metabolizing enzymes.*

Introduction

Several hundred genera are used medicinally, mainly as herbal preparations in the indigenous systems of medicine in different countries and are sources of very potent and powerful drugs. Drug discovery is very difficult task and only about one in a hundred thousand or more compounds evaluated biologically will make it to the market as a drug. This time the global population is estimated to be at least 9.2 billian. At least 80% of the World's population in developing countries uses plant materials as their source of primary health care (Cordell and Colvard, 2005). Then, even with this very incomplete database of global ethnomedical information, there is abundant opportunity for the discovery of new

medicinal agents. Hence *Terminalia belerica* Roxb. (Family: Combretaceae) commonly known as Bahera in Hindi (Kirtikar and Basu, 1933) is selected for this study. It is one of the ingredients of Ayurvedic purgative medicament of Triphala (Sivarajan, 1994). The fruit has bitter, astringent, tonic, laxative and antipyretic activity (Chopra et al., 1996) and is used traditionally for the relief of piles, dropsy, dysentery, diarrhea, leprosy and dyspepsia (Wealth of Asia, 1996). It reduces lipid level from the liver and heart, which can lower the disease risk associated with these organs (Tariq et al., 1977). Liver diseases still remain as one of the serious health problems inspite of tremendous strides in the modern medicine. Therefore there is a need to develop alternative hepatoprotective drugs. To the best of our knowledge, a report dealing with the preliminary investigation to asses its hepatoprotective effects is available against CCl_4 induced toxicity (Jadon et al., 2005) and no scientific data has been published against acetaminophen poisoning. Thus the aim of this study is to evaluate the hepatoprotective effect of *Terminalia belerica* against acetaminophen induced liver injury in rats.

Materials and methods

Preparation of the extract

Fruits of *Terminalia belerica* (TB) were procured from authenticated Ayurvedic dealer and were identified by the taxonomist of Botany Department of Jiwaji University, Gwalior. A voucher specimen (No. 336) has been deposited in herbarium (Acronym JUG). Fruits were dried in the shade, chopped and extracted with ethanol. A series of extraction was conducted to obtain ethanolic extract of *Terminalia belerica* fruits (17.6% yield w/w). An aqueous suspension was prepared in 2% gum acacia and different doses of extract (100, 200, 400 & 800 mg/kg, p.o.) were given to the animals. *Silybum marianum* (Silymarin, 50 mg/kg, p.o.) was used as a reference drug in this experiment.

Animals

Female albino rats of Sprague Dawley strain (8-10 weeks old having130$\pm$10 g b.w.) were used for this study. Animals were maintained under standard husbandry conditions (24 $\pm$ 2°C temperature, 60-70% relative humidity and 12 h photoperiod). They were fed on pellet diet (Pranav Agro Industries, New Delhi, India, having metal contents in ppm dry weight Cu 10; Mn 33; Zn 45; Co 5) and water *ad libitum*. Animals used in this study were treated and cared for in accordance with the guidelines recommended by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India,

Ministry of Culture, Chennai-India. Experimental protocol was approved by Institutional Ethical Committee (CPCSEA/501/01/A) of Jiwaji University, Gwalior-India.

Chemicals

All chemicals used in this study were of analytical grade and obtained from Sigma-Aldrich, E-Merck and Loba Chemicals Pvt. Ltd. etc. All diagnostic kits used in the experiments were procured from E-Merck.

Hepatotoxicant

Acetaminophen (2.0 g/kg, p.o. once only) (Chattopadhyay et al., 1992).

Study design

Animals were divided into seven groups of six animals each and were treated as follows:

Group 1: Normal control (vehicle only)

Group 2: Experimental control (APAP: 2.0 g/kg, p.o. once only)

Group 3: APAP + TB Extract (100 mg/kg, p.o.)

Group 4: APAP + TB Extract (200 mg/kg, p.o.)

Group 5: APAP + TB Extract (400 mg/kg, p.o.)

Group 6: APAP + TB Extract (800 mg/kg, p.o.)

Group 7: APAP + Silymarin (50 mg/kg, p.o.)

Animals were sacrificed 24 h after therapy of extract. Blood samples were withdrawn from each animal just before the necropsy by puncturing the retro-orbital venous sinus centrifuged and serum was separated for estimation of serum transaminases (Reitman and Frankel, 1957), serum alkaline phosphatase (Fiske and Subbarow, 1925), lactate dehydrogenase (Wrobleski and Due, 1955), total protein content (Lowry et al., 1951) and blood sugar (Asatoor and King, 1954). Liver of each rat were promptly excised to determined glycogen (Seifter et al., 1950), drug metabolizing enzymes ie. aniline hydroxylase (Kato and Gillette, 1965) and amidopyrine-N-demethylase (Chochin and Axelord, 1959) were estimated. Hepatic reduced glutathione was estimated using dithionitrobenzoic acid (DTNB) (Brehe and Burch, 1976). The quantitative measurement of hepatic lipid peroxidation was done by measuring the concentration of thiobarbituric acid reactive substances (TBARS) (Sharma and Krishnamurthy, 1968). Total and direct bilirubin, triglycerides, cholesterol and albumin were also determined (Kit methods, E-Merk) using Autoanalyzer (Microlab 200).

Histopathological studies

Liver tissues were collected from the large lobe for histopathological study. They were fixed in Bouin's solution for 24 h, dehydrated and embedded in paraffin. The tissue blocks were prepared and cut into 5 μm thick. These cross sections were stained using haematoxylin and eosin dyes (H&E) (E-Merck) and mounted with dibutyl polystyrine xylene (DPX) for photomicroscopic observations. For transmission electron microscopy studies, small pieces (1 mm^3) of liver were fixed in 3.2% glutaraldehyde prepared in 0.1 M phosphate buffer and they were kept at 4°C for 18 h. This was followed by washing the tissue with phosphate buffer. Post fixation of the tissue was done with 1% osmium tetraoxide solution. Then the tissues were dehydrated in acetone series and subsequently embedded in epon resin and were polymerised for 20 h at 70°C. Ultrathin sections were cut on a Reichert jung Ultracut-E Microtome, using glass knives. The sections were placed on uncoated grids and stained with uranyl acetate and lead citrate (Hayat and Arif, 1970). They were examined in a JEOL JEM 1200 EX transmission electron microscope at 80 KV.

Statistical analysis

Statistical calculations were carried out with the Graph Pad software package (Statistica, San Jose, USA). Results are expressed as the mean ± S.E.M. Student's *t*-test was used for statistical analyses. P value at 5% level was considered as significant. One-way analysis of variance (ANOVA) was done to compare the mean levels of various parameters of the different experimental groups (Snedecor and Cochran, 1994).

Results

Results of this study represented that four different doses of extract (100, 200, 400 and 800 mg/kg, p.o.) reversed in varying degree the changes induced by acetaminophen (2.0 g/kg, p.o.). AST, ALT, SALP and LDH activities were increased 3.1, 7.4, 2.5 and 3.5 folds respectively in the toxicant exposed rats. Treatment with extract at different doses showed effectiveness in a dose dependent manner. It was interesting to note that both the doses 400 and 800 mg/kg showed similar recoupment (Table 1). Hypercholesterolaemia, hyperbilirubineamia and steatosis often arises in biliary obstruction and reaches a very high level in APAP induced toxicity. Treatment with 400 and 800 mg/kg doses of extract showed significant ($P \leq 0.05$) inhibition in cholesterol, triglycerides and direct bilirubin level whereas 100 & 200 mg/kg dose of extract exhibited insignificant effect (Table 2).

A significant decrease was observed in total protein content on the other hand albumin level increased after toxicant exposure. Extract therapy (400 and 800 mg/kg) protected depletion in protein synthesis. High bolus dose of acetaminophen caused significant inhibition in blood sugar level (1.48 folds) and glycogen content (2.44 folds). Considerable recovery was seen at 400 and 800 mg/kg doses whereas 100 and 200 mg/kg doses of extract were found to be less effective. Lipid peroxidation is a highly destructive process that induces a plethora of alterations in the structure and function of cellular membrane. Results indicated that APAP accentuated the amount of malonyldialdehyde and decreased the reduced glutathione level. Treatment with extract reversed these parameters at higher doses. Results revealed that APAP caused significant ($P \leq 0.05$) inhibition in the activities of drug metabolizing enzymes such as aniline hydroxylase and amidopyrine-N-demethylase. Treatment with extract at 400 and 800 mg/kg after APAP administration showed significant recoupment in these enzymatic activities (Table 4).

Discussion

The acute toxicity produced by acetaminophen was associated with a variety of biochemical abnormalities and these could usually be attributed to the release of intracellular constituents into the circulation. APAP caused severe hepatotoxicity as indicated by sharp elevation in the activities of serum transaminases, alkaline phosphatase and lactate dehydrogenase. It indicates cellular leakage and loss of the functional integrity of cell membranes. The stabilization of these enzymes by the extract is a clear indication of the improvement of the functional status of liver cells. Other plant extracts *viz. Phyllanthus niruri* (Bhattacharjee and Sil, 2006) and *Hemidesmus indicus* Rbr. (Baheti et al., 2006) also help to replenish APAP toxicity. These findings are further corroborated with the histopathological examination by recouping centrilobular necrosis. The vulnerable effect of APAP on carbohydrate metabolism was observed by decreasing glycogen and blood sugar level. This might be attributed to failure of liver to produce glucose. Liver glycogen phosphorylase acts as the glucose sensor of liver, showing the breakdown of glycogen whenever the level of blood glucose is low. Therapy with extract showed dose dependent recovery in blood sugar and glycogen content which indicated hepatoprotective activity of extract.

A high bolus dose of paracetamol results in significant loss of the total protein content. It may be due to lipid peroxidation of cell membranes, which results in loss of

cytosolic proteins (Yeh et al., 2003). Stimulation of protein synthesis is an important therapeutic property of extract. It may be due to promotion of ribosomal assembly to facilitate uninterrupted protein biosynthesis. The cytoplasm of the cell is full of lipid vacuoles that are almost exclusively triglycerides and serve as an energy reservoir. Acetaminophen caused injury in the parenchymal cells by affecting the fat accumulation, particularly triglycerides. Blockage secretion of hepatic triglycerides into the plasma may result steatosis. Increase in the total and direct bilirubin concentration might be attributed to the failure of normal uptake, conjugation and excretion by the damaged hepatic cells. Thus hyperbilirubinaemia reflects pathophysiology of liver (Klassen et al., 1984). Treatment with extract also resulted in a decrease of serum bilirubin level. This study was also corroborated with the earlier reports on the hepatoprotective activity of *Trianthema portalacastrum* L. (Kumar et al., 2004) and *Nymphaea stellata* Willd. (Bhandarkar and Khan, 2004).

Depletion of hepatic glutathione has been constructed as evidence supporting the hypothesis that reactive metabolites generated by APAP, lead to glutathione oxidation. In addition, toxicants directly inhibit cellular proliferation, to induce oxidative stress and alter Ca^{2+} homeostasis (Bosch et al., 2006). The possible mechanisms of hepatoprotective action of TB extract may be due to its antioxidant activity as indicated by decrease in lipid peroxidation and increase of glutathione contents. Histopathological study indicated that APAP caused pathological changes in hepatocytes. This effect was seen in mitochondria, nucleus and intracellular space of liver cells. However, these pathological changes in liver cells were recouped in extract treated animals. Thus *Terminalia belerica* extract reversed various biochemical and histopathological changes produced by acetaminophen, showing significant hepatoprotective potential.

Acknowledgements

Authors are thankful to Jiwaji University, Gwalior (M.P.) and ICMR (45/8/2003/BMS/TRM) New Delhi, for financial assistance.

References

Asatoor, A.M., King, E., 1954. Simplified colorimetric blood sugar method. Biochem. J. 44, 56.

Baheti, J.R., Goyal, R.K., Shah, G.B., 2006. Hepatoprotective activity of Hemidesmum indicus Rbr. in rats. Indian J. Expt. Biol. 44 (5), 399-402.

Bhandarkar, M.R., Khan, A., 2004. Antihepatotoxic effect of Nymphaea stellata Wild. against carbon tetrachloride induced hepatic damage in albino rats. J. Ethnopharmacol. 91, 61-74.

Bhattacharjee, R., Sil, P.C., 2006. The protein fraction of Phyllanthus niruri plays a protective role against acetaminophen induced hepatic disorder via its antioxidant properties. Phytother. Res. 20(7), 595-601.

Bosch, M.E., Sanchez, A.J., Rojas, F.S., Ojeba, C.B., 2006. Determination of paracetamol: Historical evolution. J. Pharm. Biomed. Anal. 42(3), 291-321.

Brehe, J.E., Bruch, H.B., 1976. Enzymatic assay for glutathione. Anal. Biochem. 74, 189.

Chattopadhyay, R.R., Sarkar, S.K., Ganguly, S., Madda, C., Baru, T.K., 1992. Hepatoprotective activity of Ocimum sanctum leaf extract against paracetamol induced hepatic damage in rats. Indian J. Pharmacol. 24, 163-165.

Chochin, J., Axelord, J., 1959. Biochemical and pharmacological changes in the rat following chronic administration of morphine and non-morphine. J. Pharmacol. Expt. Therap. 125, 105-110.

Chopra, R.N., Nayar, S.L., Chopra, I.C., 1996. Glossary of India Medicinal Plants. CSIR Publication, New Delhi, pp. 241.

Cordell, G.A., Colvard, M.D., 2005. Some thoughts on the future of Ethnopharmacology. J. Ethnopharmacol. 100, 5-14.

Fiske, C.H., Subbarow, Y., 1925. The colorimetric determination of phosphates. J. Biological. Chem. 66, 375-380.

Hayat, A., Arif, M., 1970. Biological Applications. In: Principle and Techniques of Electron Microscopy. Van Nostrard Reinhold Company, New York.

Jadon, A., Bhadauria, M., Shukla, S., 2005. 3,4,5-trihydroxybenzoic acid and Terminalia belerica: A hepatoprotective study. Indian Drugs 42 (3), 136-143.

Kato, R., Gillette, J.R., 1965. Effect of starvation on NADPH dependent enzymes in liver microsomes of male and female rats. J. Pharmacol. Exp. Therap. 150, 279-284.

Kirtikar, K.R., Basu, B.D., 1933. Terminalia Linn, 2., 2nd Indian Medicinal Plants, Lalit Mohan Basu, Allahabad, India, pp.1014-1033.

Klaassen, C.D., Watkin, J.B., 1984. Mechanism of formation, hepatic uptake and biliary excretion. Pharmacol. Rev. 36, 1-67.

Kumar, G., Sharmila, B.G., Vanita, P.P., Sundararajan, M., Rajsekara, P.M., 2004. Hepatoprotective activity of Trianthema portuacastrum L. against paracetamol and thioacetamide intoxication in albino rats. J. Ethnopharmacol. 92(1), 37-40.

Lowry, O.H., Rosenbrough, N.J., Farr, A.L., Randall, R.J., 1951. Protein measurement with Folin's phenol reagent. J. Biological Chem. 193, 265-269.

Reitman, S., Frankel, S., 1957. A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. American J. Clinical Patho. 28, 56-63.

Seifter, S., Dayton, S., Novic, B., Muintwyler, E., 1950. The estimation of glycogen with anthrone reagent. Archives. Biochem. 25, 191-193.

Sharma, S.K., Krishnamurthy, C.R., 1968. Production of lipid peroxides of brain. J. Neurochem. 15, 147-149.

Sivarajan, V.V., 1994. Ayurvedic drugs and their plant sources. Lebanon, New Hampshire: International Science Publisher.

Snedecor, G.W., Cochran, W.G., 1994. Statistical Method. Published by Affiliated East West Press Pvt. Ltd., Iowa State University Press, Amsterdam, Iowa, (8th edn), pp. 217-236.

Tariq, M., Hussain, S.J., Asif, M., Jahan, M., 1977. Protective effect of fruit extracts of Emblica officinalis and Terminalia belerica in experimental myocardial necrosis in rats. Indian J. Expt. Biol. 15, 485-486.

Wealth of Asia. 1996. CD-ROM (D-2.3), New Delhi, NISCOM.

Wroblewski, Due, L., 1955. Colorimetric method for LDH. In: Micro-analysis in Medical Biochemistry. Wootton IDP (eds), J & A. Churchill Ltd., 104 Gloucester Place, (4th edn), pp. 115-118.

Yeh, M.L., Liu, C.F., Huang, C.L., Huang, T.C., 2003. Hepatoprotective effect of Angelica archangelica in chronically ethanol treated mice. Pharmacol. 68, 70-73.

Abbreviations

AH = Aniline hydroxylase

ALT = Alanine aminotrasferase

A-N-D = Amidopyrine-N-demethylase

ANOVA = Analysis of variance

APAP = Acetaminophen

AST = Aspartate aminotrasferase

D. Bilirubin = Direct Bilirubin

GSH = Reduced glutathione

LDH = Lactate dehydrogenase

LPO = Lipid peroxidation

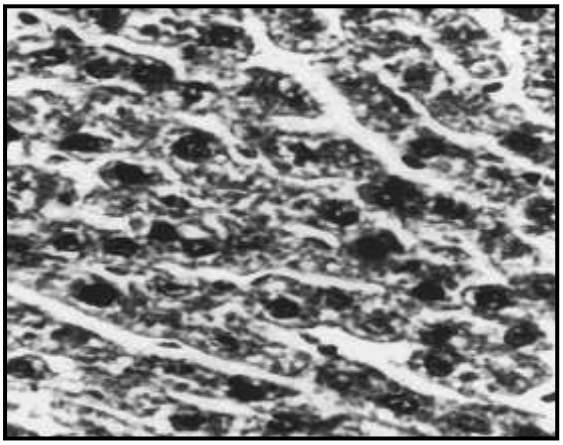
MDA = Malondialdehyde

SALP = Serum alkaline phosphatase

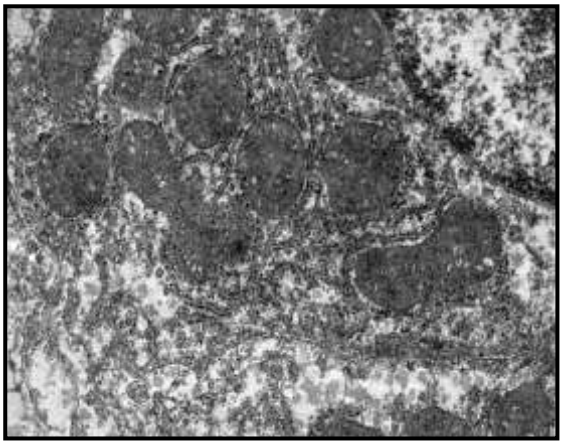
Sily = Silymarin

T. Bilirubin = Total Bilirubin

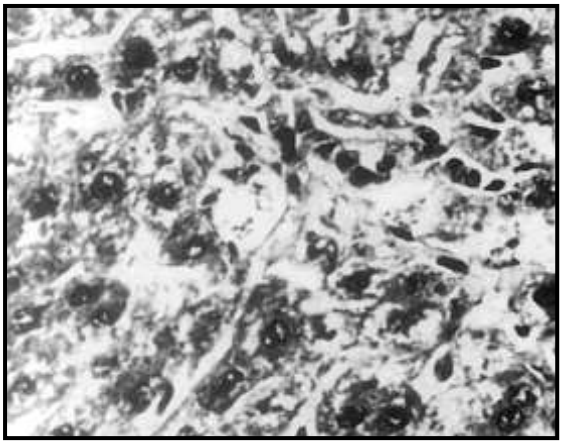
TB = *Terminalia belerica*



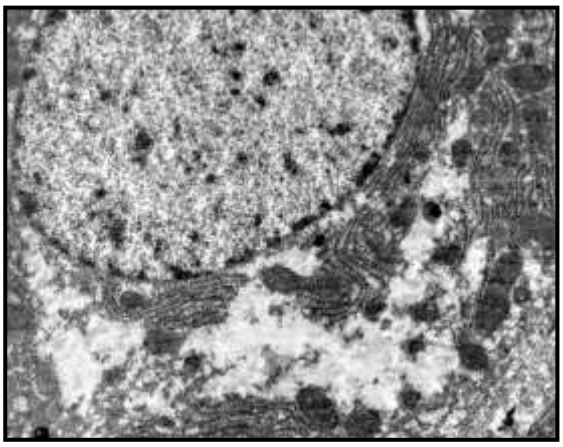
[1]



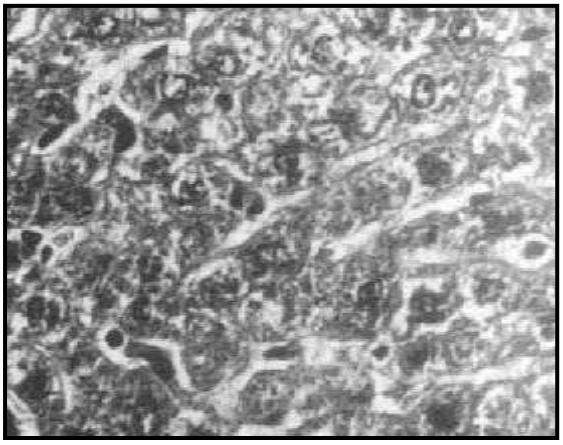
[4]



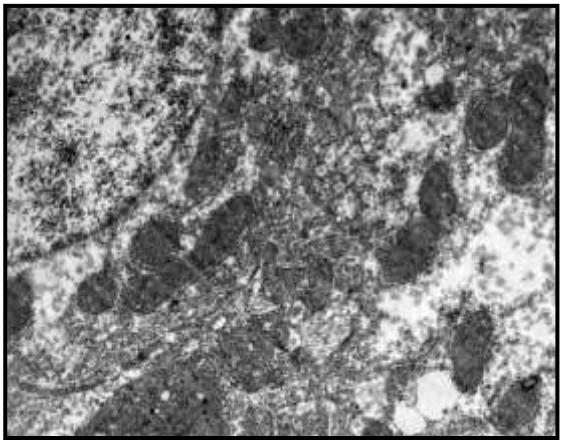
[2]



[5]



[3]



[6]

Legends of Figures

Fig. **1** Section of normal control rat liver showing normal appearance (X 400).

Fig. **2** Administration of acetaminophen. Note swollen hepatocytes, necrosis and fatty accumulation along with hyperchromatic nuclei (X 400).

Fig. **3** Treatment with *Terminalia belerica* extract (400 mg/kg, *p.o.*) showing cuboidal hepatocytes and clear sinusoidal spaces (c.f. 2) (X 400).

Fig. **4** Electron micrograph of normal control rat liver showing well formed nucleus, mitochondria, endoplasmic reticulum and glycogen particles (X 1100).

Fig. **5** Administration of APAP. Note severe vacuolation and loss of cytoplasmic matrix (X 1100).

Fig. **6** Treatment with *Terminalia belerica* extract showing well formed mitochondria along with endoplasmic reticulum and glycogen particles (X 1100).

Table 1. Effect of TB extract on liver function tests against acetaminophen induced acute toxicity in rats

Treatments	**AST**	**ALT**	**SALP**	**LDH**
	(IU/L)	**(IU/L)**	**(mg Pi/100 ml/h)**	(µ mole pyruvate/min/L)
Normal control	65.4 ± 3.42	43.0 ± 2.46	199 ± 10.4	43.0 ± 2.46
APAP (2.0 g/kg)	203 ± 13.0#	319 ± 18.3#	498 ± 27.8#	152 ± 7.46#
APAP + TB (100 mg/kg)	191 ± 17.2	293 ± 22.9	484 ± 25.7	146 ± 10.2
APAP + TB (200 mg/kg)	183 ± 10.7	259 ± 22.5	454 ± 25.7	139 ± 10.1
APAP + TB (400 mg/kg)	135 ± 9.71*	195 ± 15.5*	410 ± 27.6*	126 ± 7.36*
APAP + TB (800 mg/kg)	130 ± 8.06*	178 ± 9.23*	392 ± 22.3*	121 ± 10.3*
APAP + Sily (50 mg/kg)	99.2 ± 6.08*	89.6 ± 6.10*	276 ± 19.3*	50.8 ± 2.84*
One-way ANOVA				
F values	27.66@	50.07@	27.09@	39.40@

Values are mean ± S.E., N = 6

P ≤ 0.05 vs. normal group, * P ≤ 0.05 vs. paracetamol administered group

ANOVA (F values at 5% level) @ = Significant

Table 2. Effect of TB extract on liver function tests against acetaminophen induced acute toxicity in rats

Treatments	T. Bilirubin (mg/dl)	D. Bilirubin (mg/dl)	Triglycerides (mg/dl)	Cholesterol (mg/dl)
Normal control	0.50 ± 0.03	0.25 ± 0.02	9.80 ± 0.71	52.80 ± 2.96
APAP (2.0 g/kg)	0.80 ± 0.05#	1.45 ± 0.08#	75.7 ± 4.55#	83.16 ± 4.35#
APAP + TB (100 mg/kg)	0.78 ± 0.05	1.35 ± 0.11	68.33 ± 4.17	79.10 ± 4.88
APAP + TB (200 mg/kg)	0.72 ± 0.52	1.30 ± 0.10	62.33 ± 3.55*	71.33 ± 4.23
APAP + TB (400 mg/kg)	0.68 ± 0.49	1.20 ± 0.06*	56.33 ± 3.00*	63.33 ± 3.62*
APAP + TB (800 mg/kg)	0.65 ± 0.05	1.16 ± 0.08*	50.83 ± 2.65*	60.16 ± 3.64*
APAP + Sily (50 mg/kg)	0.50 ± 0.36*	0.38 ± 0.02*	23.83 ± 1.48*	53.80 ± 3.25*
One-way ANOVA				
F values	7.43@	43.42@	70.21@	11.27@

Values are mean ± S.E., N = 6

P ≤ 0.05 vs. normal group, * P ≤ 0.05 vs. paracetamol administered group

ANOVA (F values at 5% level) @ = Significant

Table 3. Effect of TB extract on liver function tests against acetaminophen induced acute toxicity in rats

Treatments	S. Proteins (mg/100 mg)	Albumin (mg/100 mg)	Blood Sugar (mg/100 g)	Glycogen (mg/100 g)
Normal control	38.0 ± 1.72	3.0 ± 0.15	110.8 ± 7.05	3200 ± 168
APAP (2.0 g/kg)	16.9 ± 0.94#	4.8 ± 0.36#	74.00 ± 4.01#	1309 ± 93.1#
APAP + TB (100 mg/kg)	19.4 ± 1.36	4.4 ± 0.31	84.20 ± 4.52	1423 ± 83.0
APAP + TB (200 mg/kg)	22.8 ± 1.38*	4.2 ± 0.35	89.75 ± 5.73*	2018 ± 160*
APAP + TB (400 mg/kg)	27.3 ± 2.57*	4.0 ± 0.29	98.8 ± 5.11*	2350 ± 230*
APAP + TB (800 mg/kg)	29.8 ± 2.15*	3.9 ± 0.29	100.0 ±5.23*	2403 ± 227*
APAP + Sily (50 mg/kg)	39.1 ± 2.56*	3.0 ± 0.17*	107.0 ± 5.59*	2905 ± 157*
One-way ANOVA				
F values	24.71@	6.44@	6.98@	20.99@

Values are mean ± S.E., N = 6

P ≤ 0.05 vs. normal group, * P ≤ 0.05 vs. paracetamol administered group

ANOVA (F values at 5% level) @ = Significant

Table 4. Effect of Tb extract on lipid peroxidation, reduced glutathione and drug metabolizing enzymes against acetaminophen induced acute toxicity in rats

Treatments A-N-D	**LPO (n mole MDA/mg protein)**	**GSH (µmole/g)**	**AH (units/ liver/mg protein) (units/g liver/mg protein)**
Normal control	0.29 ± 0.01	6.48 ± 0.36	33.8 ± 2.45
6.50 ± 0.50			
APAP (2.0 g/kg)	0.72 ± 0.05#	4.05 ± 0.24#	14.8 ± 0.83#
3.60 ± 0.18#			
APAP + TB (100 mg/kg)	0.62 ± 0.03	4.23 ± 0.28	15.2 ± 0.90
3.68 ± 0.25			
APAP + TB (200 mg/kg)	0.58 ± 0.04	4.64 ± 0.26	16.3 ± 1.00
3.75 ± 0.27*			
APAP + TB (400 mg/kg)	0.52 ± 0.04*	4.86 ± 0.26*	17.7 ± 0.90*
4.25 ± 0.20*			
APAP + TB (800 mg/kg)	0.49 ± 0.03*	4.91 ± 0.26*	18.7 ± 1.11*
4.34 ± 0.26*			
APAP + Sily (50 mg/kg)	0.34 ± 0.02*	5.90 ± 0.29*	33.8 ± 2.40*
6.08 ± 0.32*			
One-way ANOVA			
F values	21.26@	11.12@	29.96@
18.50@			

Values are mean ± S.E., N = 6

P ≤ 0.05 vs. normal group, * P ≤ 0.05 vs. paracetamol administered group

ANOVA (F values at 5% level) @ = Significant