Original Paper

Protective Effect of *Solanum trilobatum* Extract in Paracetamol-induced Liver Toxicity

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ABSTRACT

Paracetamol is a widely used over-the-counter analgesic and antipyretic agent. But the excessive use of paracetamol can damage multiple organs, especially liver and kidney. Paracetamol-induced liver toxicity is more severe in alcoholics.

Solanum trilobatum is a South Indian climbing plant belonging to the family Solanaceae, and is used traditionally in Siddha system of medicine to treat various diseases. The purpose of this study was to find out whether there is any liver protective effect for this plant extract in paracetamol-induced toxicity.

The study was conducted at Medical College, Thiruvananthapuram, Kerala. The plant material collected from the tribal region of Tirunelveli was taxonomically identified by the Deptof Botany, Karyavattam University Campus, Thiruvananthapuram. With a soxlet extractor, coarsely powdered plant parts of *Solanum trilobatum* was extracted using 90% alcohol. Five groups of 6 albino rats each were used for the study. The protective effect of two oral doses of the alcoholic extract of *Solanum trilobatum* suspended in 0.1% CMC in paracetamol-induced liver toxicity was analysed in comparison with the known liver protective agent silymarin and untreated control group.

The biochemical data were statistically analysed using the Student *t* test. Histopathology of rat liver and biochemical parameters revealed significant hepatoprotective effect of this extract in paracetamol-induced liver toxicity.

Key Words: Paracetamol; *Solanum trilobatum*; Hepatotoxicity; Liver toxicity

Introduction

Paracetamol is a widely used over-the-counter analgesic and antipyretic agent. But the excessive use of paracetamol can damage multiple organs, especially liver and kidney. In both organs, toxicity is not from the drug itself but from its metabolite N-acetyl-p-benzoquinoneimine (NABQI).[1] Treatment is aimed at removing paracetamol from the body and replacing glutathione. N-acetylcysteine acting as a precursor for glutathione helps the body to regenerate it in enough amounts to prevent damage to liver. But liver transplant is required if damage to the liver becomes severe. Paracetamol-induced liver toxicity is more severe in alcoholics.[2]

Solanum trilobatum is a South Indian climbing plant belonging to the family Solanaceae. It has been used traditionally in Siddha system of medicine to treat various diseases.[3] The purpose of this study was to find out whether there is any liver protective effect of this plant extract in paracetamol induced toxicity.

Materials and Methods[4,5]

This study was conducted at Medical College, Thiruvananthapuram. The plant material was collected from the tribal region of Tirunelveli. Taxonomical identification of the plant was conducted by the Dept of Botany, Karyavattam University Campus, Thiruvananthapuram. The plant parts were air dried for three weeks.

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With a soxlet extractor, coarsely powdered plant parts of *Solanum trilobatum* were extracted using 90% alcohol. Permission for the study was obtained from the Institutional Animal Ethics Committee (IAEC). Acute toxicity study of the extract was conducted initially to determine the dose to be selected for further studies.[6] Healthy adult albino rats of either sex were used for determining the liver protective effect of the extract. As the extract was only partially soluble in distilled water, a suspension of the extract in 0.1% CMC was used for oral administration to rats. They were maintained on standard diet and water *ad libitum*, and were randomly allotted into 5 groups of 6 each as:

- Group A - Negative control, i.e., treated with only the vehicle, 0.1% CMC orally for 7 days.
- Group B - Reference group to produce paracetamol-induced toxicity.
- Group C - Positive control, i.e., treated with a known liver protectant, silymarin in a dose of 25 mg/kg orally for 7 days.[7]
- Group D - Test group treated with 400 mg/kg of the extract orally for 7 days.
- Group E - Test group treated with 800 mg/kg of the extract orally for 7 days.

On the 7th day, paracetamol suspension was given orally in a dose of 750 mg/kg to all rats except those in group A. After 48 hrs following the last dose, blood was collected from all animals by puncturing the retro-orbital plexus for estimating biochemical parameters. The blood was allowed to clot for 45 minutes at room temperature. Serum was separated by centrifugation at 2500 rpm for 30 minutes. With the help of an autoanalyser, biochemical parameters such as SGOT, SGPT, SLAP, serum bilirubin and total protein were analysed. The data were statistically analyzed using the Student *t* test, and *P* values of standard and test were calculated by comparing with the groups receiving paracetamol only. After drawing the blood samples, the rats were sacrificed and livers were excised quickly and fixed in 10% formalin. Paraffin sections were prepared, stained with haematoxylin and eosin and finally mounted in neutral DPX medium. Histopathological examinations were subsequently done.

Results

When administered at a dose of 750 mg/kg, paracetamol-induced hepatic damage was evident from the histopathology of rat liver and from the biochemical parameters. Reference group (Group B) developed necrosis of liver cells and fatty degeneration (**Fig 1**).

Liver cells of normal control group (Group A) not administered paracetamol, having normal appearance were used for comparison (**Fig 2**)

When protected with the hepatoprotective agent silymarin (**Fig 3**), Group3 showed normal hepatic cell regeneration.

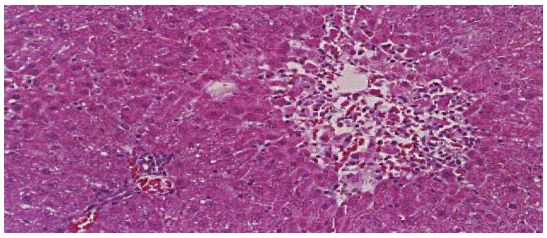

Fig 1 Paracetamol treated group

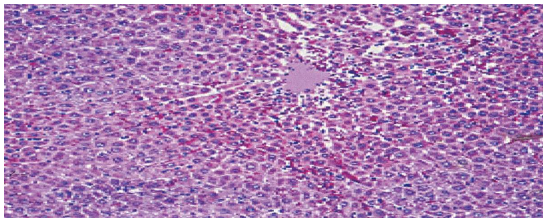

Fig 2 Normal control

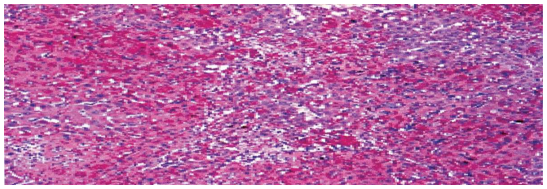

Fig 3 Silymarin + paracetamol

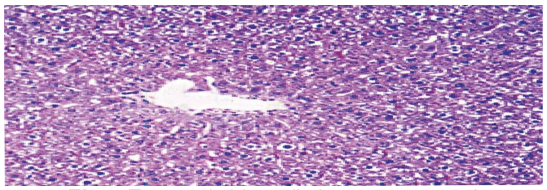

Fig 4 Extract (400 mg/kg) + paracetamol

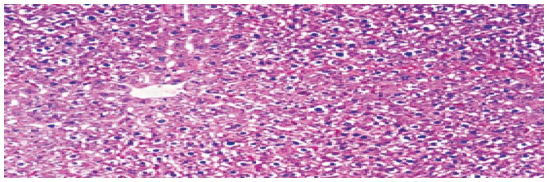

Fig 5 Extract (800 mg/kg) + paracetamol

The test compound *Solanum trilobatum Linn* extract exhibited dose-dependent hepatoprotective effect. The groups receiving 400 mg/kg extract and paracetamol showed normal liver cell regeneration, though some fatty changes were present (**Fig 4**). The groups receiving 800 mg/kg extract and paracetamol showed normal pattern with clear hepatic cells and prominent nucleus (**Fig 5**).

The hepatoprotective effect of *Solanum trilobatum* extract is evident from the biochemical parameters also. The groups administered paracetamol alone, i.e., Group B showed considerable hike in the levels of SGOT, SGPT, alkaline phosphatase, total bilirubin, etc. Treatment with 400 mg/kg and 800 mg/kg of *Solanum trilobatum* extract produced significant reduction in these values when analysed by the student t test (**Tables 1-4**).

Table 1

Group	SGOT (IU/L)	SD	Mean±SEM	*t* value	p value
Normal liver	124.8; 120.86 122.35; 122.14 118.28; 120.56	2.176	121.49±0.88		
Paracetamol treated	256.32; 267.34 268.11; 259.77 272.32; 259.28	6.266	263.85±2.55		
Silymarin + Paracetamol treated	122.32; 121.4 123.85; 122.72 120.54; 122.7	1.152	122.25±0.47	54.44	<0.0001
Extract 400 mg + Paracetamol treated	201.33; 198.44 195.48; 183.22 202.67; 199.5	7.087	196.77±2.89	17.37	<0.0001
Extract 800 mg + Paracetamol treated	132.33; 141.08 137.72; 135.25 137.54; 134.69	3.474	135.93±1.42	43.73	<0.0001

Table 2

Group	SGPT (IU/L)	SD	Mean+SEM	t value	p value
Normal liver	105.63; 105.85 103.12; 102.93 103.55; 104.28	1.263	104.22±0.51		
Paracetamol treated	239.45; 214.86 218.39; 236.44 219.66; 227.32	10.137	226.02±4.14		
Silymarin + Paracetamol treated	101.41; 104.25 102.13; 102.08 105.34; 102.05	1.548	102.87±0.63	29.41	<0.0001
Extract 400 mg + Paracetamol treated	183.22; 174.63 172.34; 173.22 178.3; 180.26	4.304	176.99±1.75	10.9	<0.0001
Extract 800 mg + Paracetamol treated	111.55; 118.26 119.35; 114.17 115.58; 116.04	2.81	115.82±1.15	25.65	<0.0001

Discussion

In this study using albino rats, the alcoholic extract of *Solanum trilobatum Linn* was found to be very effective in reversing paracetamol-induced liver damage. Preliminary phytochemical studies of this extract have revealed the presence of flavonoids in it. Flavonoids act as antioxidants by scavenging free radicals. Hence, the hepatoprotective effect of *Solanum trilobatum* may be due to the presence of flavonoids in the extract.[8,9]

As liver is the primary site for biotransformation of drugs, it is highly prone to their toxic effects. Alcoholism, which is steadily on the rise in Kerala, increases the chances for liver toxicity from therapeutic drugs. For example paracetamol, though a time-tested drug, can cause fatal hepatic failure if used in excess, especially in alcoholics. If daily administration of this plant extract can reverse the liver toxicity, it could be a boon to those who have to take high doses of these drugs for different ailments.

Table 3

Group	Total Bilirubin (mg/dl)	SD	Mean+SEM	*t* value	p value
Normal liver	0.88; 0.94 0.85; 0.84 0.82; 0.80	0.05	0.85±0.02		
Paracetamol treated	2.11; 2.15 1.96; 1.9 2.05; 2.33	0.152	2.08±0.06		
Silymarin + Paracetamol treated	0.87; 0.93 0.95; 0.93 0.92; 0.9	0.0311	0.92±0.01	18.45	<0.0001
Extract 400 mg + Paracetamol treated	1.3; 1.22 0.98; 0.99 1.25; 1.15	0.135	1.14±0.05	11.23	<0.0001
Extract 800 mg + Paracetamol treated	0.99; 0.98 0.94; 0.96 1.1; 0.97	0.056	0.99±0.02	16.48	<0.0001

Table 4

Group	SALP(IU/l)	SD	Mean+SEM	*t* value	p value
Normal liver	208.63; 205.36 206.57; 209.68 209.04; 207.95	1.62	207.87±0.66		
Paracetamol treated	404.55; 401.22 405.08; 408.33 404.18; 402.55	2.42	404.32±0.99		
Silymarin + Paracetamol treated	198.35; 196.24 197.38; 198.4 200.54; 196.87	1.51	197.96±0.62	176.61	<0.0001
Extract 400 mg + Paracetamol treated	313.32; 311.33 305.54; 302.57 301.46; 300.96	5.28	305.86±2.12	41.44	<0.0001
Extract 800 mg + Paracetamol treated	226.64; 238.45 233.25; 229.1 228.34; 220.55	6.06	229.38±2.47	65.59	<0.0001

However, the present study was conducted by administering only two doses of the extract each for 7 days. The minimum dose/frequency of the extract required for reversing paracetamol-induced toxicity is not clearly understood from this study. Similarly, the study does not give any idea of whether the extract has any beneficial effect in an alcoholic person taking hepatotoxic drugs. But, as the compound has shown significant hepatoprotective effect, it is important to study the active constituents and their exact mechanism of action in more detail by future research.

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