

## HEPATOPROTECTIVE ACTIVITY OF POLYHERBAL *CURNA* (CHURNA) ON ETHANOL MEDIATED PARACETAMOL INDUCED HEPATOTOXICITY IN RATS

Dr. Venu Sampath Kumar Golla\*

A.U. College of Pharmaceutical Sciences, Andhra University, Visakhapatnam,  
Andhra Pradesh, India.

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### \*Corresponding Author

Dr. Venu Sampath  
Kumar Golla

A.U. College of  
Pharmaceutical Sciences,  
Andhra University,  
Visakhapatnam, Andhra  
Pradesh, India.

### ABSTRACT

Ethanol is widely used drink in beverages and paracetamol is widely used drug throughout the world. Among the chronic alcoholics Paracetamol induced hepatotoxicity is very severe. The present study was extended to the combined model of ethanol and paracetamol because in order to combat the severe hepatotoxicity produced by combined effect of ethanol and paracetamol, no single plant derivative or isolated active principle is sufficient. Hence a polyherbal formulation of mixture of plant derived products is essential. The polyherbal churna was prepared by mixing dried aqueous extract powders of barks of *Alstonia scholaris*, *Ficus bengalensis*, *Pongamia pinnata* and *Ricinus communis* in equal quantities. The prepared churna was evaluated for hepatoprotective activity against the

paracetamol and ethanol induced hepatotoxicity. The hepatic damage in rats was evidenced by elevated levels of SGPT, SGOT, ALP, Total protein and Total bilirubin. Ethanol mediated Paracetamol induced hepatotoxicity was treated with churna showed significant activity by comparing with silymarin and the results were further supported by histopathological studies.

**KEYWORDS:** Hepatoprotective activity, polyherbal churna, Ethanol, Paracetamol, Silymarin.

### INTRODUCTION

Nature is the best combinatorial chemist and possibly has answers to all diseases of mankind. Till now, natural product compounds discovered from medicinal plants (and their analogues thereof) have provided numerous clinically useful drugs (Jachak S.M.et al., 2007). Liver is

the largest organ in the body with a median weight of 1800 gms in men and 1400 gms in women. The basic functional unit of liver is the liver lobule, a cylindrical structure, several millimeters in length and 0.8 mm and 2 mm in diameter. The human liver contains 50,000 to 1, 00,000 lobules. The liver lobule is constructed around a central vein which empties into a hepatic venule than the hepatic vein finally into the inferior vena cava. The hepatic lobule is roughly a hexagonal arrangement of plates of hepatocytes radiating outward from a central vein in the center.

## **MATERIAL AND METHODS**

### **Preparation of Churna**

Churna is a fine powder of drugs. The selected plant bark aqueous extract was dried and were subjected to fine particles. The dried plant bark extracts of **Alstonia scholaris**, **Ficus bengalensis**, **Pongamia pinnata** & **Ricinus communis** are mixed together in equal proportion.

### **Oral administration**

For administration of vehicle/toxicant/suspension of functional foods/silymarin an oral feeding needle attached to a syringe was used. The needle was curved and round tipped. The animals were positioned securely by holding the backside skin of the neck with left hand and the oral feeding needle was introduced through intradental space right into the esophagus and the substances were administered to the respective groups by pushing the plunger of the syringe. Then the needle was withdrawn slowly and smoothly (Ghosh MN, 2005). In acute toxicity studies no mortality was observed at 2000mg/Kg bd.wt. of Churna. Hence 2000mg/Kg was considered as cutoff dose and 1/20<sup>th</sup>, 1/10<sup>th</sup> & 1/5<sup>th</sup> dose of this cutoff value was taken for further study.

### **The biochemical parameters**

Serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), Serum alkaline phosphatase (ALP), Serum total protein, Serum total bilirubin.

### **Biological parameters and methods**

Liver function tests which include liver enzymes are grouped for tests that are designed to give information about the state of liver. In the present study the following serum biochemical parameters have been selected to assess the liver function in rats.

**Liver function tests used in the study**

1. Determination of serum glutamate pyruvate transaminase (SGPT/ALT)
2. Determination of serum glutamate oxaloacetate transaminase (SGOT/AST)
3. Determination of serum alkaline phosphatase (ALP)
4. Determination of serum total bilirubin
5. Determination of total protein.

**Collection of blood samples from rats****Material required**

1. Microcentrifuge tubes (1.5 ml capacity).
2. Microcapillary tubes (1 mm diameter).
3. Absorbent cotton.

Blood was collected from the retro orbital plexus of rats (RileyV., 1960). A fine capillary was inserted gently in the inner angle of the eye and then the capillary was pushed under the eye ball at 45 degree angle and over the bony socket to rupture the fragile venous capillary of the ophthalmic venous plexus. The Passage is about 10 mm. The tip of the capillary tube should be held gently merely resting on fingers while blood was flowing after collecting the desired volume, capillary was removed with simultaneous release of pressure by forefingers and thumb. Any residual blood droplet around the eye ball was wiped off by dry cotton wool.

**Methods of Estimation**

Quite a large number of enzymes estimations are available which are used to ascertain liver function. But most commonly and routinely employed methods in laboratories are estimations of SGPT, SGOT, ALP, cholesterol and bilirubin.

**1. Assay of serum glutamate pyruvate transaminase (SGPT/ALT)**

ALT is present in high concentration in the liver and to a lesser extent in kidney, skeletal muscle, pancreas, spleen and lungs. Increased levels are generally a result of liver diseases such as cirrhosis, carcinoma, viral or toxic hepatitis and obstructive jaundice.

**2. Assay of serum glutamate oxaloacetate transaminase (SGOT) or AST**

(Kamei T. et al.) AST occurs in all human tissues and is present in large amounts in liver, renal, cardiac and skeletal muscle tissue. Increased levels are associated with liver diseases or damage, myocardial infarction, muscular dystrophy and chole`cystitis.

### 3. Assay of Serum Alkaline Phosphatase (ALP)

ALP is present in high concentration in liver, bone, placenta, intestine and certain tumours. Increased levels of the enzyme occur in liver diseases, bone diseases (Rickets, Paget's Diseases), Hodgkin's diseases or congestive heart failure.

### 4. Assay of serum Bilirubin (Jendrassik, L. et al.)

Bilirubin is a breakdown product of hemoglobin. Bilirubin formed in the reticulo-endothelial system is transported to the liver bound to albumin. This Bilirubin is water insoluble and is known as indirect or unconjugated Bilirubin. In the liver, Bilirubin is conjugated to glucuronic acid to form direct Bilirubin, conjugated Bilirubin is excreted via the biliary system into the intestine where it is metabolized by bacteria to urobilinogen and stercobilinogen.

### 5. Estimation of serum total protein

#### Biuret Method (Gomall, A.G., & Doumas, B.T., et al)

The Biuret Method, which is the most widely used method for total protein determination, relies on the complexation of  $\text{Cu}^{++}$  by the function groups involved with the peptide bond. A minimum of two peptide bonds is needed for the complexation to occur. Upon complexation, a violet color is observed. The absorbance of the  $\text{Cu}^{++}$ -protein complex is measured at 540 nm and compared to a standard curve.

#### Statistical analysis

Results were expressed as mean  $\pm$  SEM, N=6). Statistical analysis was performed with one way analysis of variance (1 way ANOVA) followed by Turkey test. P value less than 0.05 was considered to be statistically significant. \*= $P < 0.05$ , \*\*= $P < 0.01$  and \*\*\*= $P < 0.001$ , when compared with toxicant group.

#### Procedure

In this method albino Wister rats of either sex weighing between 150-250 g were used for study. The rats were housed under standard conditions of constant temperature and lighting (12 hours light/dark cycle). They had access to standard pellet diet (Gold Mohur Lipton India Ltd.) and water ad libitum. The rats were selected and divided into 11 groups each containing six rats. Paracetamol, powders of selected functional foods and silymarin were dissolved in 2% gum acacia suspension. The treatment protocol was planned to study the effect of functional foods in curative aspect of paracetamol induced hepatotoxicity (Shenoy AK et al.,

2002). The dose of PCM to induce hepatic damage was selected as 2 g/kg body weight for three days (Shenoy AK et al., 2002). The doses of the plants were selected as 200 mg/kg (LD) and 400 mg/kg (HD) of body weight. The dose of silymarin used was 100 mg/kg BW (Setty SR et al., 2007). The treatment protocol is summarized and given below.

### Group 1

Normal control, 2 % w/v gum acacia suspension orally, 1ml/kg once daily for 7 days.

### Group 2

Ethanol 3.7 g/kg for 7 days and on 8<sup>th</sup> day Paracetamol 2g/kg followed by 1ml/kg of 2 % w/v gum acacia once daily p.o from 8<sup>th</sup> day to 14<sup>th</sup> day.

### Group 3

Ethanol 3.7 g/kg for 7 days and on 8<sup>th</sup> day Paracetamol 2g/kg followed by 100mg/kg dose of *churna* once daily p.o from 8<sup>th</sup> day to 14<sup>th</sup> day.

### Group 4

Ethanol 3.7 g/kg for 7 days and on 8<sup>th</sup> day Paracetamol 2g/kg followed by 200mg/kg dose of *churna* once daily p.o from 8<sup>th</sup> day to 14<sup>th</sup> day.

### Group 5

Ethanol 3.7 g/kg for 7 days and on 8<sup>th</sup> day Paracetamol 2g/kg followed by 400mg/kg dose of *churna* once daily p.o from 8<sup>th</sup> day to 14<sup>th</sup> day.

### Group 6

Ethanol 3.7 g/kg for 7 days and on 8<sup>th</sup> day Paracetamol 2g/kg followed by 100mg/kg dose of Silymarin once daily p.o from 8<sup>th</sup> day to 14<sup>th</sup> day.

On 0<sup>th</sup> day (one day before the dosing) and 15<sup>th</sup> day blood was collected retro-orbital puncture from all the animals. Serum was separated by centrifugation (3000 rpm for 15 min.) and subjected for estimation of biochemical parameters such as SGPT, SGOT, ALP, serum cholesterol and bilirubin, as described in chapter 3. Then the 15<sup>th</sup> day the animals were sacrificed and the livers were isolated and washed with fresh saline. Livers were stored in 10% formalin for histopathological study.

## RESULTS

### 1. Aspartate aminotransferase levels (AST or SGOT)

The dose of 2g/kg body weight of Paracetamol induced significant increase in SGOT levels with an increase of 112.92% (92.62 IU/L to 197.21 IU/L) compared to normal control where the increase was 2.15% (88.96 IU/L to 90.87 IU/L). ETH + PCM induced serum rise of SGOT was protected by 100mg/kg, 200mg/kg and 400mg/kg bd. wt doses of *churna* in a dose dependent manner and by 100mg/kg dose of Silymarin. The rise in SGOT levels in animals treated with 100mg/kg dose of *churna* showed 74.56% rise (90.17 IU/L to 187.40 IU/L), animals treated with 200mg/kg dose of *churna* showed 50.26% rise (88.08 IU/L to 132.35 IU/L), animals treated with 400mg/kg dose of *churna* showed 14.65% rise (88.99 IU/L to 102.03 IU/L), where as the standard Silymarin at a dose of 100mg/kg showed 12.37% rise (86.07 IU/L to 96.72 IU/L). The results were compiled in table nos. 1, 2, 3 and graphically represented in histogram nos. 1 & 6.

### 2. Alanine aminotransferase levels (ALT or SGPT)

The dose of 2g/kg body weight of Paracetamol induced significant increase in SGPT levels with an increase of 229.55% (32.39 IU/L to 106.74 IU/L) compared to normal control where the increase was 5.33% (30.39 IU/L to 32.01 IU/L). ETH + PCM induced serum rise of SGPT was protected by 100mg/kg, 200mg/kg and 400mg/kg bd. wt doses of *churna* in a dose dependent manner and by 100mg/kg dose of Silymarin. The rise in SGPT levels in animals treated with 100mg/kg dose of *churna* showed 156.00% rise (30.55 IU/L to 78.21 IU/L), animals treated with 200mg/kg dose of *churna* showed 85.23% rise (35.49 IU/L to 65.74 IU/L), animals treated with 400mg/kg dose of *churna* showed 21.96% rise (33.43 IU/L to 40.77 IU/L), where as the standard Silymarin at a dose of 100mg/kg showed 6.66% rise (44.87 IU/L to 42.07 IU/L). The results were compiled in table nos.1, 2, 3 and graphically represented in histogram nos. 2 & 6.

### 3. Alkaline Phosphatase levels (ALP)

The dose of 2g/kg body weight of Paracetamol induced significant increase in ALP levels with an increase of 140.98% (184.53 IU/L to 444.69 IU/L) compared to normal control where the increase was 0.093% (193.26 IU/L to 193.08 IU/L). ETH + PCM induced serum rise of ALP was protected by 100mg/kg, 200mg/kg and 400mg/kg bd. wt doses of *churna* in a dose dependent manner and by 100mg/kg dose of Silymarin. The rise in ALP levels in animals treated with 100mg/kg dose of *churna* showed 50.06% rise (180.51 IU/L to 270.87 IU/L),

animals treated with 200mg/kg dose of churna showed 18.23% rise (182.84 IU/L to 216.17 IU/L), animals treated with 400mg/kg dose of churna showed 11.74% rise (186.86 IU/L to 208.80 IU/L), where as the standard Silymarin at a dose of 100mg/kg showed 2.06% rise (192.65 IU/L to 196.63 IU/L).

#### 4. Total Protein

The dose of 2g/kg body weight of Paracetamol induced significant increase in total protein levels with an decrease of 45.79% (9.52 IU/L to 5.16 IU/L) compared to normal control where the decrease was 2.28% (9.00 IU/L to 9.21 IU/L). ETH + PCM induced serum rise of total protein was protected by 100mg/kg, 200mg/kg and 400mg/kg bd. wt doses of *churna* in a dose dependent manner and by 100mg/kg dose of Silymarin. The rise in total protein levels in animals treated with 100mg/kg dose of churna showed 24.14% decrease (8.66 IU/L to 6.57 IU/L), animals treated with 200mg/kg dose of churna showed 8.87% decrease (9.70 IU/L to 8.84 IU/L), animals treated with 400mg/kg dose of churna showed 5.46% decrease (8.97 IU/L to 8.48 IU/L), where as the standard Silymarin at a dose of 100mg/kg showed 4.26% decrease (8.45 IU/L to 8.09 IU/L). The results were compiled in table nos. 1, 2, 3 and graphically represented in histogram nos. 4 & 6.

#### 6. Total Bilirubin

The dose of 2g/kg body weight of Paracetamol induced significant increase in total bilirubin levels with an increase of 46.80% (0.94 IU/L to 0.50 IU/L) compared to normal control where the increase was 8.42% (0.95 IU/L to 0.87 IU/L). ETH + PCM induced serum rise of total bilirubin was protected by 100mg/kg, 200mg/kg and 400mg/kg bd. wt doses of *churna* in a dose dependent manner and by 100mg/kg dose of Silymarin. The rise in total bilirubin levels in animals treated with 100mg/kg dose of churna showed 28.42% rise (0.95 IU/L to 0.68 IU/L), animals treated with 200mg/kg dose of churna showed 35.80% rise (0.81 IU/L to 0.52 IU/L), animals treated with 400mg/kg dose of churna showed 27.16% rise (0.81 IU/L to 0.59 IU/L), where as the standard Silymarin at a dose of 100mg/kg showed 33.33% rise (0.87 IU/L to 0.58 IU/L). The results were compiled in table nos. 1, 2, 3 and graphically represented in histogram nos. 5 & 6.

**Table No. 1: levels of serum biochemical parameters in rats for ETH+PCM induced hepatotoxicity on 0 day (Prior to treatment) in Curative study.**

G	TREATMENT	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	TOTAL PROTEIN (g/dl)	TOTAL BILIRUBIN (mg/dl)
1	2% Gum acacia(1ml/kg;p.o)	88.96±3.19	30.39±3.01	193.26±4.56	9.00±0.70	0.95±0.07
2	3.7g/kg Ethanol + 2g/kg dose of PCM	92.62±1.82	32.39±3.15	184.53±6.14	9.52±0.67	0.94±0.05
3	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg Churna	90.17±4.56	30.55±1.10	180.51±5.08	8.66±1.11	0.95±0.09
4	3.7g/kg Ethanol + 2g/kg dose of PCM+200mg/kg Churna	88.08±4.00	35.49±2.53	182.84±3.30	9.70±0.68	0.81±0.05
5	3.7g/kg Ethanol + 2g/kg dose of PCM+400mg/kg Churna	88.99±2.28	33.43±1.79	186.86±4.36	8.97±0.37	0.81±0.07
6	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg Silymarin	86.07±4.17	44.87±7.13	192.65±3.50	8.45±0.55	0.87±0.05

Values are expressed as Mean ± SEM

**Table No. 2: Levels of serum biochemical parameters in rats for ETH+PCM induced hepatotoxicity on 15<sup>th</sup> day of treatment in Curative study.**

G	TREATMENT	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	TOTAL PROTEIN (g/dl)	TOTAL BILIRUBIN (mg/dl)
1	2% Gum acacia(1ml/kg;p.o)	90.87±2.78	32.01±3.04	193.08±4.46	9.21±0.96	0.87±0.21
2	3.7g/kg Ethanol + 2g/kg dose of PCM	197.21±7.42	106.74±4.79	444.69±23.63	5.16±0.40	0.50±0.03
3	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg Churna	157.40±4.67***	78.21±2.31***	270.87±7.77***	6.57±0.75	0.68±0.08
4	3.7g/kg Ethanol + 2g/kg dose of PCM+200mg/kg Churna	132.35±6.99***	65.74±2.00***	216.17±4.78***	8.84±0.77***	0.52±0.07
5	3.7g/kg Ethanol + 2g/kg dose of	102.03±2.18***	40.77±1.59***	208.80±7.23***	8.48±0.36**	0.59±0.06

	PCM+400mg/kg <i>Churna</i>					
6	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg Silymarin	96.72±4.65***	42.07±2.77***	196.63±5.20***	8.09±0.53**	0.58±0.09

Values are expressed as Mean ± SEM, Significance \*\*\*p<0.001when compared to ETH+PCM control.

Table No. 3: Average % change of serum biochemical parameters in rats for ETH+PCM induced hepatotoxicity on 15<sup>th</sup> day of treatment in Prophylactic study.

G	TREATMENT	SGOT (IU/L)	SGPT (IU/L)	ALP (IU/L)	TOTAL PROTEIN (g/dl)	TOTAL BILIRUBIN (mg/dl)
1	2% Gum acacia(1ml/kg;p.o)	2.15	5.33	0.093	2.28	8.42
2	3.7g/kg Ethanol + 2g/kg dose of PCM	112.92	229.55	140.98	45.79	46.80
3	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg <i>Churna</i>	74.56	156.00	50.06	24.14	28.42
4	3.7g/kg Ethanol + 2g/kg dose of PCM+200mg/kg <i>Churna</i>	50.26	85.23	18.23	8.87	35.80
5	3.7g/kg Ethanol + 2g/kg dose of PCM+400mg/kg <i>Churna</i>	14.65	21.96	11.74	5.46	27.16
6	3.7g/kg Ethanol + 2g/kg dose of PCM+100mg/kg Silymarin	12.37	6.66	2.06	4.26	33.33

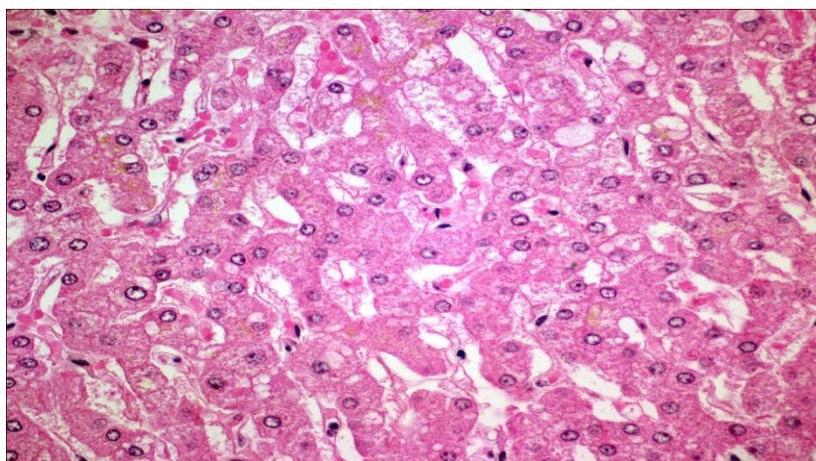
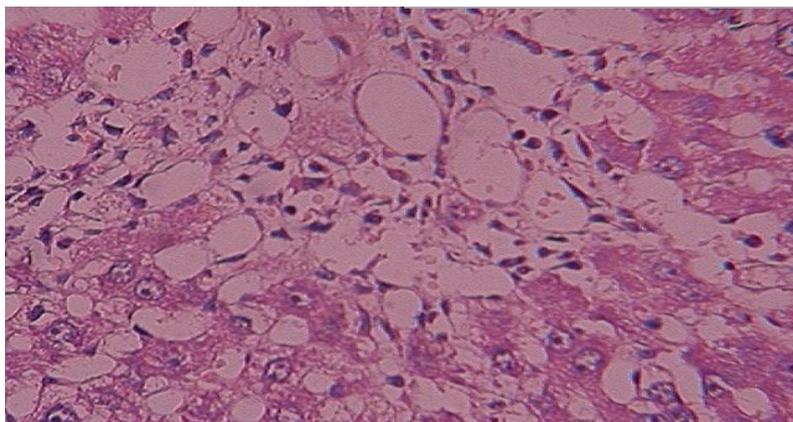
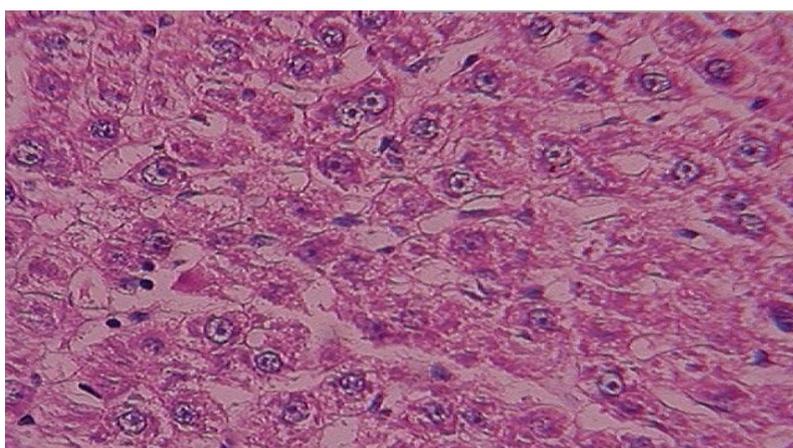


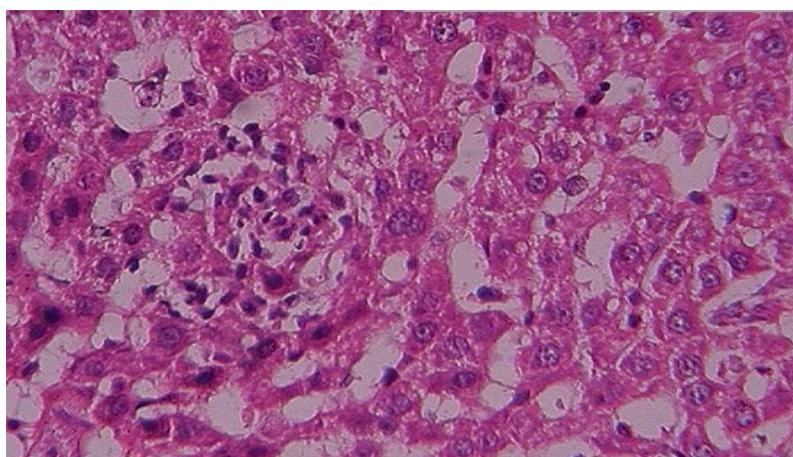
Fig. No. 1: Normal Control in ETH + PCM Induced Hepatotoxicity in Rats.



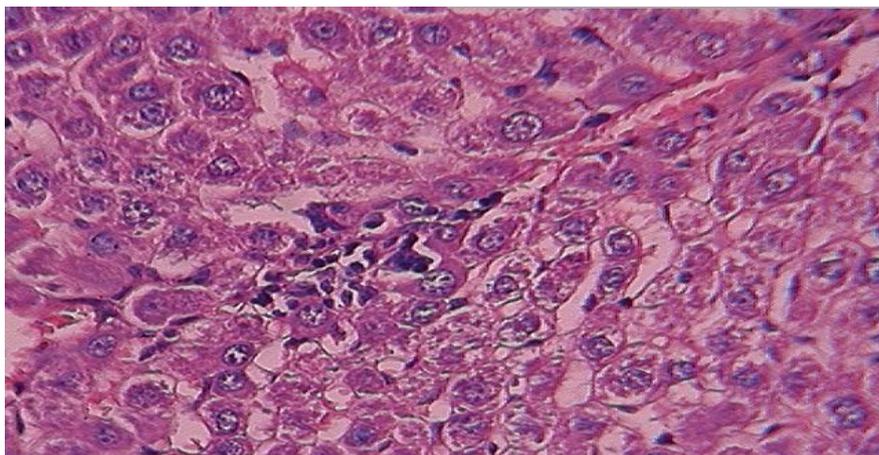
**Fig. No. 2:** ETH for 14 days 3.7gm/Kg bd. wt + PCM 2gm/Kg bd. wt. On 15<sup>th</sup> day.



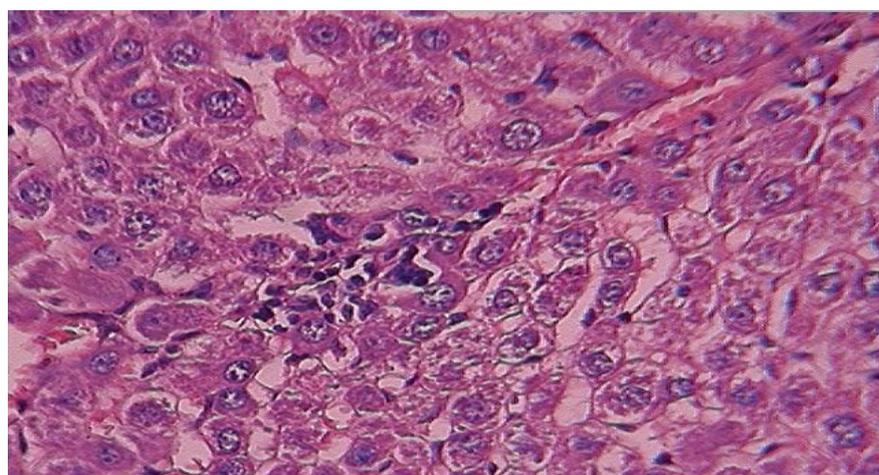
**Fig. No. 3:** ETH for 14 days 3.7gm/Kg bd. wt and 100 mg/Kg bd.wt. of Churna for 14 days+ PCM 2gm/Kg bd.wt. On 15<sup>th</sup> day.



**Fig. No. 4:** ETH for 14 days 3.7gm/Kg bd. wt and 200mg/Kg bd.wt. of churna for 14 days+ PCM 2gm/Kg bd.wt. On 15<sup>th</sup> day.



**Fig. No. 5:** ETH for 14 days 3.7gm/Kg bd. wt and 400mg/Kg bd.wt. of churna for 14 days + PCM 2gm/Kg bd.wt. On 15<sup>th</sup> day.



**Fig. No. 6:** ETH for 14 days 3.7gm/Kg bd. wt and 100mg/Kg bd. wt. of Silymarin For 14 days+ PCM 2gm/Kg bd.wt. On 15<sup>th</sup> day.

### Histopathological Studies

**Group 1:** In normal control group Hepatic globular structure was found to be normal. (Fig No.1).

**Group 2:** Treatment with ETH+PCM (Toxic control group) showed around 75% of cellular fatty infiltration, derangement of cords and necrosis have been observed (Fig No.2).

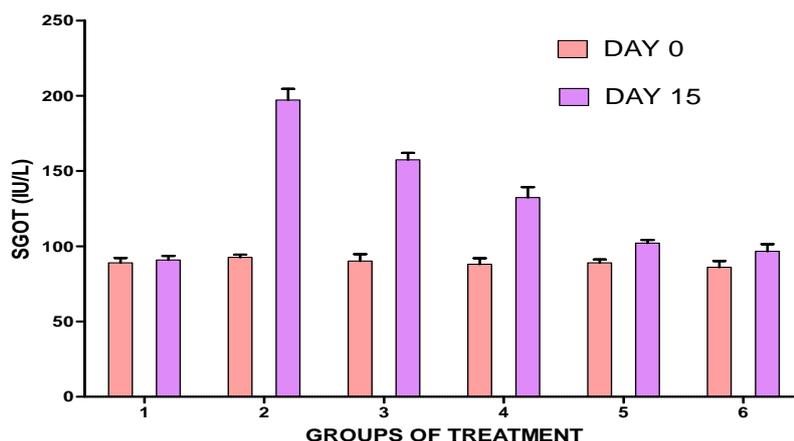
**Group 3:** Treatment with 100mg/Kg.bd.wt of Churna showed less than 50% of cellular infiltration, mild regeneration with binucleated hepatocytes. (Fig No.3).

**Group 4:** Treatment with 200 mg/Kg.bd.wt of Churna showed less than 25 % of cellular fatty infiltration, necrosis and moderate regeneration with binucleated hepatocytes. (Fig No.4).

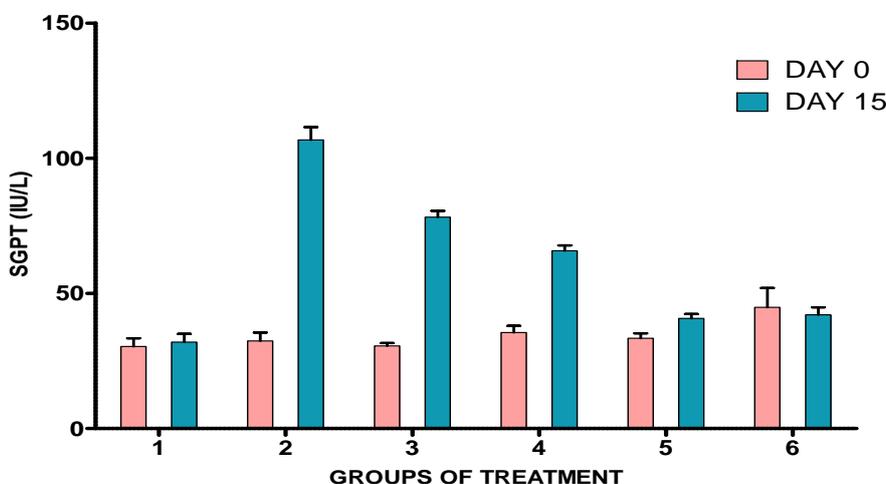
**Group 5:** Treatment with 400mg/Kg.bd.wt of Churna showed less than 25 % of cellular fatty infiltration, necrosis and good regeneration with binucleated hepatocytes. (Fig No.5).

**Group 6:** Treatment with 100mg/Kg.bd.wt of Silymarin showed good regeration with normal features of hepatocytes. (Fig No.6).

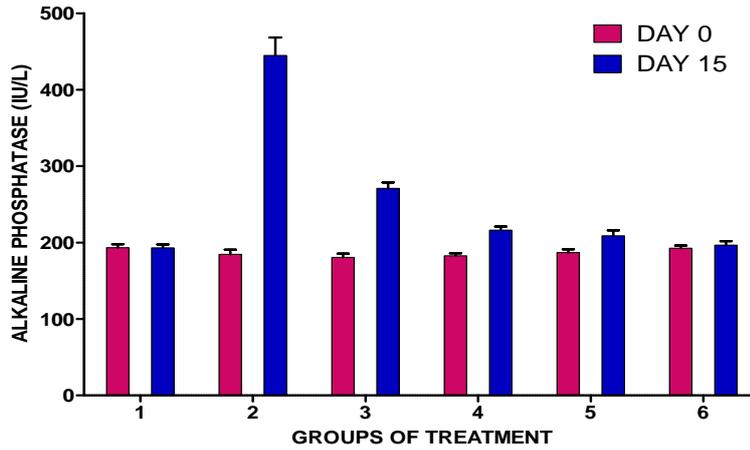
**Histopathology of churna treated rats {curative}**



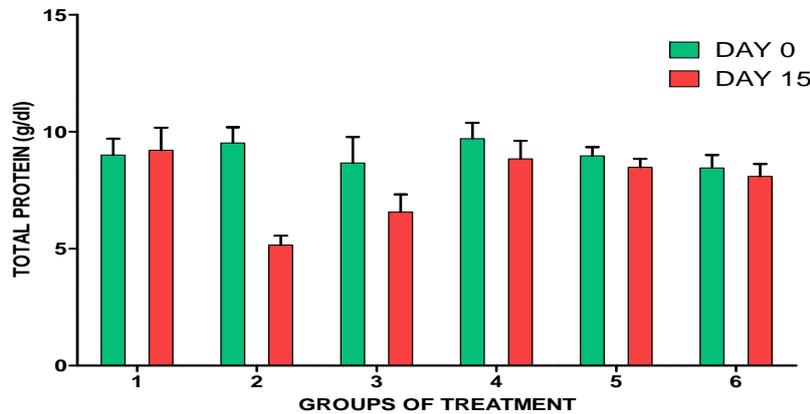
**Histogram No. 1: SGOT in PCM induced hepatotoxicity in rats (Curative study with “Churna”).**



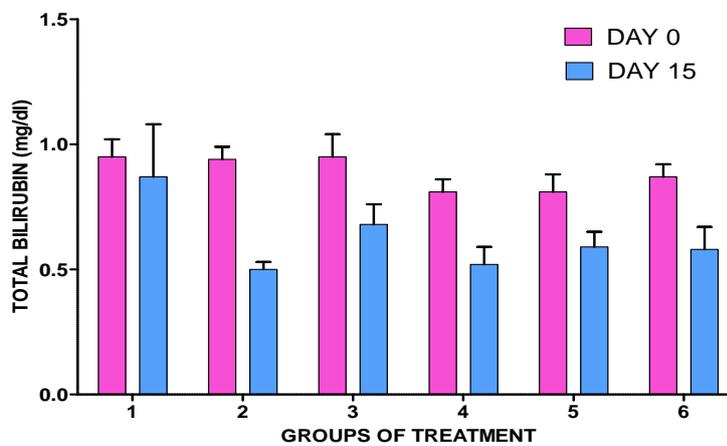
**Histogram No. 2: SGPT in PCM induced hepatotoxicity in rats (Curative study with “Churna”).**



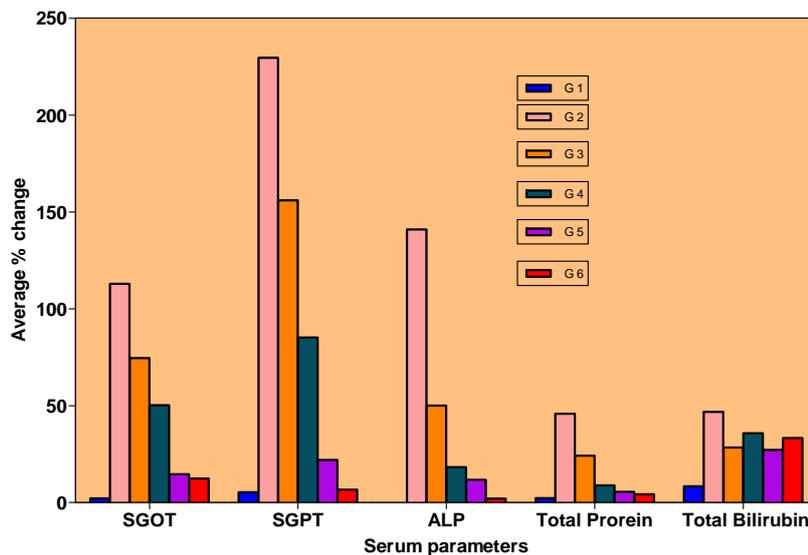
**Histogram No. 3: ALP in PCM induced hepatotoxicity in rats (Curative study with "Churna").**



**Histogram No. 4: Total Protein in PCM induced hepatotoxicity in rats (Curative study with "Churna").**



**Histogram No. 5: Total Bilirubin in PCM induced hepatotoxicity in rats (Curative study with "Churna").**



**Histogram No. 6: Average % change of Serum biochemical parameters in ETH+PCM induced hepatotoxicity in rats (Curative study).**

## DISCUSSION

In the estimation of hepatic damage by paracetamol and ethanol combined treatment, the same parameters were used which were used in previous studies. In the present study 3.7 g/kg bd.wt. of Ethanol and 2g/kg bd.wt. of Paracetamol was used to induce hepatotoxicity in both prophylactic and curative treatment. A sharp rise in the serum biochemical parameters like SGPT, SGOT, ALP, Total bilirubin and total protein have been observed in toxicant group (Group-2) compared to normal control. The elevated levels of the above serum enzymes were reduced by the treatment of Churna in prophylactic and curative treatment in a dose dependent manner.

In this study, Churna was prepared by the mixing of dried extract bark powder of *Alstonia scholaris*, *Ficus bengalensis*, *Pongamia pinnata* and *Ricinus communis* in equal amount. The Churna was administered along with 2% gum acacia suspension. The three doses i.e 100mg, 200mg and 400mg/Kg.bd.wt were selected and used as previous studies. Silymarin 100mg/Kg. bd. wt. was taken as standard. The 400 mg/Kg bd. wt. of Churna showed comparable effect with that of Silymarin. As compared to the individual hepatoprotective activity of selected plant bark extract, the hepatoprotective activity of the polyherbal Churna showed better result. As polyherbal Churna have protective activity against both the mechanism i.e. lipid peroxidation responsible for Paracetamol toxicity and free radical generation for ethanol toxicity work together in toxicity produced by combined model.

The Histopathological study also reported the biochemical evidence for the hepatoprotection shown by the Churna the normal hepatic features (Naidu R.S et al., 2007) were found in normal control group. In ethanol mediated Paracetamol treated group (Group-2) all the normal features of the hepatic cell were modified and there was hepatic necrosis, cellular infiltration, macrovaculolar steatosis, fatty infiltration with ballooning and derangement of cords was observed. In case of Churna and Silymarin treated groups the normal structures were protected in both prophylactic and curative study in a dose dependent manner with minor abnormalities. From the above results we have conclude that polyherbal formulation as Churna have both improved free radical scavenging activity and lipid peroxidation activity than the single selected plant bark extract.

### CONCLUSION

The poly herbal churna showed dose dependent activity in treatment of ethanol mediated paracetamol induced Toxicity. This study showed that the treatment with poly herbal churna of plant bark extracts treatment is very effective like silymarin. The histo-pathological studies also supported the results of the poly herbal churna in the treatment of hepatic disorders.

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