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HEPATOPROTECTIVE ACTIVITY OF PANCHAGAVYA GHRITA AGAINST CARBONTETRACHLORIDE INDUCED HEPATOTOXICITY IN RATS

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ABSTRACT *Objective:* To investigate the hepatoprotective activity of Panchagavya Ghrita (PG) against CCl₄ induced hepatotoxicity.

Methods: The hepatoprotective activity of PG was tested against carbontetrachloride induced hepatotoxicity in albino rats. The degree of protection was determined by measuring levels of serum marker enzymes like serum glutamate oxaloacetate transaminase (SGOT) serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP) and acid phosphatase (ACP). The histological studies were also carried out. Silymarin was used as the standard drug for comparison.

Results: Administration of Panchagavya Ghrita (150-300 mg/kg, *p.o.*) markedly prevented CCl₄ induced elevation of levels of serum GPT, GOT, ACP and ALP. The results are comparable to that of silymarin. A comparative histopathological study of liver exhibited almost normal architecture, as compared to control group.

Conclusion: Treatment with Panchagavya Ghrita significantly reduced the CCl₄ induced hepatotoxicity. A comparative histological study of liver from different groups further confirmed the hepatoprotective activity of Panchagavya Ghrita.

KEY WORDS Marker enzymes CCl₄ liver enzymes

INTRODUCTION

Panchagavya is a term used in Ayurveda to describe five important substances obtained from cow namely urine, dung, milk, ghee and curd. A number of formulations mentioned in Ayurveda describes the use of Panchagavya components either alone or in combination with drugs of herbal, animal or mineral origin¹. Recently US Patent was obtained by CSIR, India which claimed a novel pharmaceutical composition containing cow urine distillate and an antibiotic². Cow urine concoction (CUC) is a popular Nigerian herbal preparation containing cow urine. Over fifty components have been identified in CUC. Its major pharmacological actions include anticonvulsant and hypoglycemic effects³. Fulzele *et al.* reported immunostimulant activity of Ashtamangal ghrita⁴, immunomodulatory activity of

Haridradi ghrita⁵ and antiinflammatory activity of Jatyadi ghrita⁶.

Panchagavya ghrita (PG) is also one of the formulations mentioned in Ayurveda which is prepared with all five components of Panchagavya viz cow milk, ghee, urine, dung and curd in equal proportions and is claimed to be useful against liver disorders, fever, inflammations, anemia and also as a rejuvenator⁷. However, scientific data are not available regarding pharmacological aspects of Panchagavya ghrita, nor are there any scientific data, which could corroborate the claims. Much work has not been carried out on biochemical, pharmacological and pharmaceutical aspects and also on chemistry of bioactive compounds in Panchagavya. Therefore it was thought worthwhile to investigate hepatoprotective activity of Panchagavya ghrita against CCl₄ induced hepatotoxicity.

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MATERIALS AND METHODS

Panchagavya ghrita (PG): The formulation was obtained as a gift sample for research from Go-Vigyan Anusandhan Kendra, Deolapar. The formulation was used as received for the present investigation.

Quality control parameters: The quality control parameters of PG were recorded by methods specified by Bureau of Indian Standards⁸. The parameters calculated were slip point, acid, free fatty acid, saponification, peroxide, iodine and ester values. The formulation appeared reasonably stable at room temperature.

Animals: Male albino rats of Sprague Dawley strain weighing 150-200 g were used for the study. The animals were housed in clean metabolic cages and maintained in controlled temperature ($27\pm 2^{\circ}\text{C}$) and light cycle (12 h light and 12 h dark). They were fed with standard pellet diet (Goldmohor brand, Lipton India Ltd.) and water *ad libitum*. The protocol was approved by Institutional Animal Ethics Committee constituted for the purpose.

Experimental: Rats were divided into 5 groups of 6 animals each as follows - Group I served as control and received subcutaneous administration of liquid paraffin (LP) only (3 ml/kg) on alternate day for one week. Liver damage was induced in remaining groups by administering CCl_4 subcutaneously in the lower abdomen in a suspension of LP in the ratio 1:2 v/v at the dose of 1 ml CCl_4 /kg body weight of each animal. Group II rats received LP+ CCl_4 on alternate days for a week by subcutaneous route. Group III received silymarin (100 mg/kg, *p.o.*) daily and LP + CCl_4 subcutaneously on alternate days for a week. Group IV and V were fed orally with Panchagavya ghrita (150 and 300 mg/kg respectively) daily and LP+ CCl_4 (*s.c.*) on alternate days for a week. The doses of Panchagavya ghrita were selected on the basis of doses prescribed by expert Ayurvedic physicians and in Ayurvedic texts. On 8th day blood was withdrawn from all groups and serum separated for estimating the levels of marker enzymes *viz* glutamate oxaloacetate transaminase (GOT)⁹ glutamate pyruvate transaminase (GPT)⁹, alkaline phosphatase (ALP)¹⁰ and acid phosphatase (ACP)¹⁰.

After sacrificing the animals, the liver was rapidly excised and serially sectioned. The tissue was fixed

Table 1. Quality control parameters of Panchagavya ghrita.

Slip point	37.0 - 37.5°C
Acid value	2.06 \pm 0.0035
Free fatty acid value	1.03 \pm 0.0018
Saponification value	98.33 \pm 1.147
Peroxide value	4.365 \pm 0.048
Iodine value	35.55 \pm 0.14
Ester value	96.275 \pm 1.15

The values are mean of 5 readings \pm SD.

in 10% formalin and consecutive sections were stained by haematoxylin and eosin for histological examination.

Statistical analysis: The data obtained were analyzed using one-way ANOVA followed by Dunnett's test. The level of significance was set at $P < 0.05$.

RESULTS

Quality control parameters: The analysis of the formulation reveals the values (Table 1) for the respective parameters.

Serum marker enzymes: The level of marker enzymes *viz* - SGPT, SGOT, ACP and ALP were elevated in CCl_4 treated group as compared to control (Table 2). The group treated with PG showed significant decrease in the levels of serum marker enzymes as compared with CCl_4 treated group.

Histopathology: The CCl_4 induced histopathological changes in liver were confirmed. Silymarin and PG reversed the liver to normalcy (Figure 1a-d).

DISCUSSION

Rapid loss of a variety of microsomal enzymic activities accompany peroxidative decomposition of lipids of liver cell endoplasmic reticulum. Disintegration of lysosomes has been correlated with peroxidative decomposition of lysosomal lipids. Peroxidative decomposition of hepatocellular membrane lipids result in breakdown of the delicate and complex mechanisms responsible for formation of VLDL in the cell, their movement within the cell and eventual extrusion into the plasma. This supposition

Table 2. Effects of Panchagavya ghrita on different biochemical parameters in the serum of rats.

Treatment		GPT (units/ml)	GOT (units/ml)	Total acid phosphatase ACP (K.A. units)	Alkaline phosphatase ALP (K.A. units)
Control group		32.83± 4.88	46.33±9.72	4.16±0.25	11.12±0.53
CCl ₄		126.33± 6.88*	114.33±6.88*	12.25±0.32*	21.21±0.53*
Silymarin (100 mg/kg orally) +CCl ₄		47.00± 6.16*	59.33±6.31*	6.34±0.27*	13.86±0.50*
PG (150 mg/kg, orally)+CCl ₄		111.50± 7.79*	86.66±11.36*	10.7±0.59*	18.96±0.54*
PG (300 mg/ kg, orally)+CCl ₄		84.6± 6.31*	78.83±3.96*	7.77±0.41*	15.78±0.58*
One-way ANOVA	F	226.97	65.27	423.83	240.56
	P	<0.0001	<0.0001	<0.0001	<0.0001

Values are expressed as mean±SD of 6 animals in each group; df=4,25

*P<0.01 as compared with group I; *P<0.01 as compared with group II (Dunnett's test).

Figure 1. Effect of Panchagavya ghrita treatment on CCl₄ induced histopathological changes in rat liver.

Figure 1a. Normal control rat: Section of liver showing normal hepatic cells.

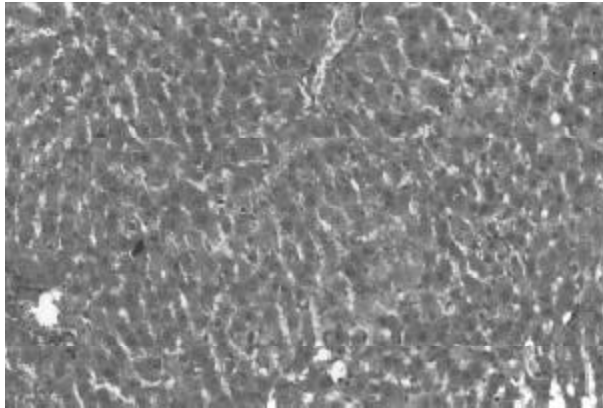


Figure 1b. CCl₄ treated rat: Section of liver showing centrilobular fatty degeneration, coludy swelling and necrosis of hepatic cells.

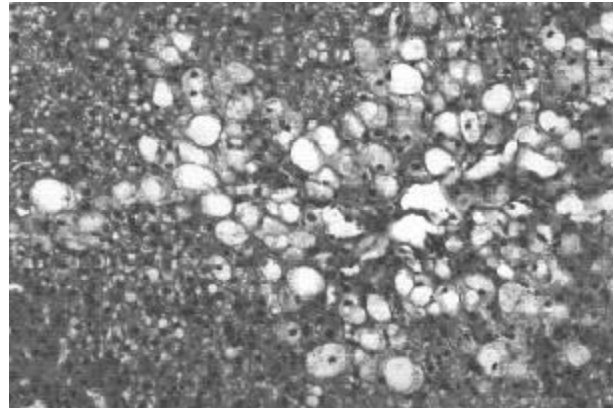


Figure 1c. Silymarin treated rat: Section of liver showing normalcy of hepatic cells, central vein and portal triad.

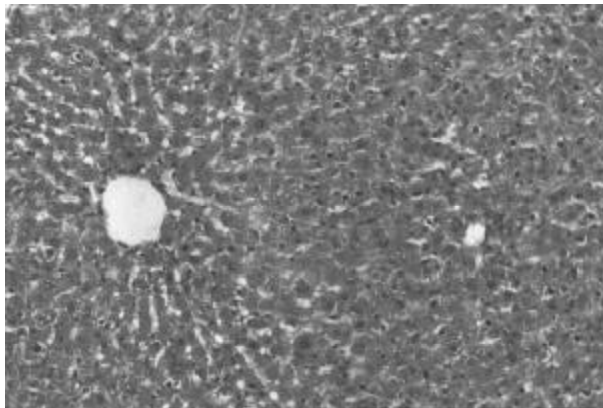
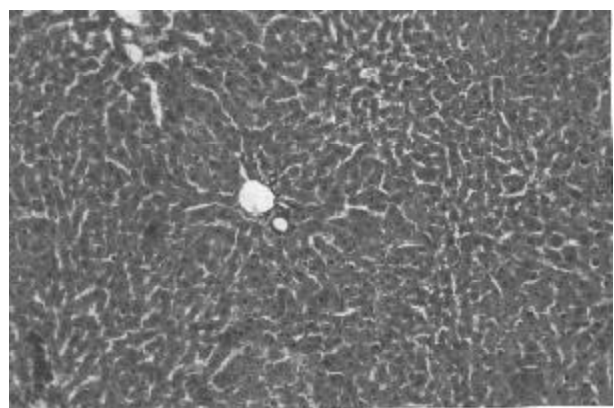


Figure 1d. Panchagavya ghrita (300 mg/kg) treated rats: Section of liver showing normalcy of hepatic cells.



is central to the lipoperoxidation theory of CCl₄ liver damage^{11,12}. Carbon tetrachloride is biotransformed by cytochrome P-450 system to produce the trichloromethyl free radical which causes lipoperoxidation. The administration of the hepatotoxicant, CCl₄ increases the serum level of marker enzymes GPT, GOT, ACP and ALP indicating the induction of hepatotoxicity. Measurement of serum enzyme levels has provided a powerful tool for studies of hepatotoxicity. It has been employed in testing for toxicity of agents whose effects are unknown and in studying the circumstances and factors which influence the effects of known hepatotoxicants like CCl₄^{13,14}. Treatment with PG in doses (150-300 mg/kg) significantly prevented the rise in the levels of serum marker enzymes *viz* GPT, GOT, ACP and ALP and the results obtained were comparable with those of silymarin treated group. The repair mechanisms are influenced by phospholipids coupled with a rise in the thymidylate synthetase and thymidine kinase levels in liver reaching a peak at 72 h indicating liver regeneration¹⁵. Both the damage and recovery proceeded simultaneously. However it is inhibited by repeated doses of CCl₄¹⁶. The comparative histo-pathological studies of liver from different groups further corroborated the hepatoprotective efficacy of PG. It would be reasonable to lay down the quality control parameters for such product since there is lack of standardized methodology in modern literature.

These findings are important from clinical point of view and need further studies to reveal the mechanism of action. It also indicates the necessity to explore experimentally similar other formulations described in ancient texts.

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REFERENCES

- Shah E. Herbal compositions. US Patent 5 693 327. 1997 Dec 2.
- Khanuja SPS. Pharmaceutical composition containing cow urine distillate and an antibiotic. US Patent 6410059. 2002 Jun 25.
- Oyebola DD. Cow's urine concoction: Pharmacological actions and mode of lethality. *Afr J Med Med Sci*1983;**12**: 57-63.
- Fulzele SV, Bhurchandi PM, Kanoje VM, Joshi SB, Dorle AK. Immunostimulant activity of *Ashtamangal ghrita* in rats. *Indian J Pharmacol* 2002;**34**:194-7.
- Fulzele SV, Satturwar PM, Joshi SB, Dorle AK. Study of immunomodulatory activity of *Haridradi ghrita* in rats. *Indian J Pharmacol* 2003;**35**:51-4.
- Fulzele SV, Satturwar PM, Joshi SB, Dorle AK. Studies of anti-inflammatory activity of a polyherbal formulation *Jatyadi ghrita*. *Indian Drugs*2002;**39**:42-4.
- Shastri AD. *Shushrut samhita*. 11th ed. Varanasi: Chaukhamba Sanskrit Prakashan; 1998. p. 410.
- Methods of sampling and tests for ghee. 4th ed. New Delhi: Published by Bureau of Indian Standards, Manak Bhawan; 1990.
- Reitman S, Frankel AS. A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminase. *American J Clin Pathol* 1957;**28**:53-6.
- Kind PRN, King AJ. Elimination of plasma phosphate by determination of hydrolysed phenol with aminoantipyrine. *J Clin Pathol*1954;**7**:322-6.
- Plaa GL. Chlorinated methanes and liver injury: Highlights of past 50 years. *Annu Rev Pharmacol Toxicol* 2000;**40**:42-65.
- Recknagel RO, Glende EA, Ugazio G, Koch RR, Srinivasan S. New data in support of the lipid peroxidation theory for carbon tetrachloride liver injury. International symposium on hepatotoxicity. 1973, March 25-30; Tel Aviv, Israel.
- Zimmerman HJ. Serum enzyme measurement in experimental hepatotoxicity. International symposium on hepatotoxicity. 1973, March 25-30; Tel Aviv, Israel.
- Buwa S, Patil S, Kulkarni PH, Kanase A. Hepatoprotective activity of *Abhrak bhashma*, an Ayurvedic drug in albino rats against hepatitis induced by CCl₄. *Ind J Exp Biol* 2001;**39**:1022-7.
- Dobrynina OV, Migushina VL, Shatinina SZ, Boldonova NB. Use of phospholipids to repair rats liver membranes during CCl₄ poisoning. *Biull Eksp Biol Med* 1987;**104**:301-5.
- Devershi P, Kanase A, Kanase R, Mane S, Patil S, Varute AT. Effect of Mandur Bhashma on lipolytic activities of liver, kidney and adipose tissue of albino rats during CCl₄ induced hepatic injury. *J Biosci* 1986;**10**:227-32.