

Effect of *Bramhi Ghrita* on Carbon Tetrachloride-Induced Hepatic Damage in Rats

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In the present study the hepatoprotective activity of *Bramhi Ghrita* was tested against carbon tetrachloride-induced hepatotoxicity in rats. The degree of protection was determined by measuring levels of serum marker enzymes, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and acid phosphatase. Histopathological studies were also carried out to support the above parameters. *Bramhi Ghrita* is a formulation that belongs to the *panchagavya* class of Ayurvedic formulations in which one or more of the five products obtained from cow (milk, *ghee*, curd, urine and dung) are used in combination with herbs. The formulation was administered at doses 100 mg/kg and 300 mg/kg/day to rats. *Bramhi ghrita* significantly reduces levels of serum marker enzymes serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and acid phosphatase elevated due to carbon tetrachloride-induced hepatotoxicity. A comparative histopathological study of liver from different groups further corroborated the hepatoprotective activity of *Bramhi Ghrita*.

In the traditional system of Ayurvedic treatment medicines consists of plant products either single drug or in combination with others which are considered to be less toxic and free from side effects compared to synthetic drugs¹. *Bramhi Ghrita* (BG) is an Ayurvedic *panchagavya* formulation containing *Bacopa monneri*, *Acorus calamus*, *Saussurea lappa*, *Evolvulus alsinoids* and cow's *ghee*. BG belongs to the *panchagavya* class of Ayurvedic formulation since it contains cow's *ghee* as one of the ingredient. *Panchagavya* is a term used in Ayurveda to describe five products obtained from cow namely milk, *ghee*, curd, urine and dung. These products, either alone or in combination with drugs of herbal, animal or mineral origin are used for the treatment of several diseases²⁻⁵. *Bacopa monneri* is reported for its sedative, tranquilising⁶⁻⁷, memory enhancer⁸, hepatoprotective⁹ and antioxidant effect¹⁰. *Acorus calamus* is reported for its carminative¹¹, sedative and tranquilising activity¹², *Saussurea lappa* is reported for antiulcer¹³, antiinflammatory¹⁴, immunostimulant¹⁵, antispasmodic, hypotensive and respiratory depressant action¹⁶. *Evolvulus alsinoids* is claimed for its use as a brain tonic, sedative, anthelmintic, antiepileptic and against leucoderma¹⁷. Traditionally cow's *ghee* is believed to increase intelligence and immunity.

Scientific data regarding pharmacological studies on BG is scant hence the screening of BG for hepatoprotective effect was carried out in the present investigation.

BG was obtained as a gift sample for research from Go-vigyan Anusandhan Kendra, Nagpur and used as received. The plant material was authenticated by a qualified botanist and the voucher specimens of plant material has been deposited in Go-vigyan Anusandhan Kendra, Nagpur. Male Wistar rats (150-200 g) were used in this study. Rats were housed under standard conditions of temperature ($23 \pm 1^\circ$) 12 h light/dark cycle and fed with standard pellet diet (Gold Mohor, Lipton India Ltd., Mumbai) and water *ad libitum*. The protocol for animal experimentation was approved by the Institutional Animal Ethical Committee. Rats were divided into 4 groups of 6 animals each as follows, Group I animals served as control and received subcutaneous administration of liquid paraffin (LP, 3 ml/kg). Liver damage was induced in the remaining groups by administering CCl_4 subcutaneously as a suspension in LP in the ratio 1:2 v/v at the dose of 1 ml CCl_4 /kg body weight of each animal. Group II animals received LP+ CCl_4 (subcutaneous route). Group III and IV were fed orally with BG at doses 100 mg/kg and 300 mg/kg and LP+ CCl_4 (s.c. route). Subsequently after 8th d treatment blood samples were collected by puncturing retro-orbital plexus of rats and

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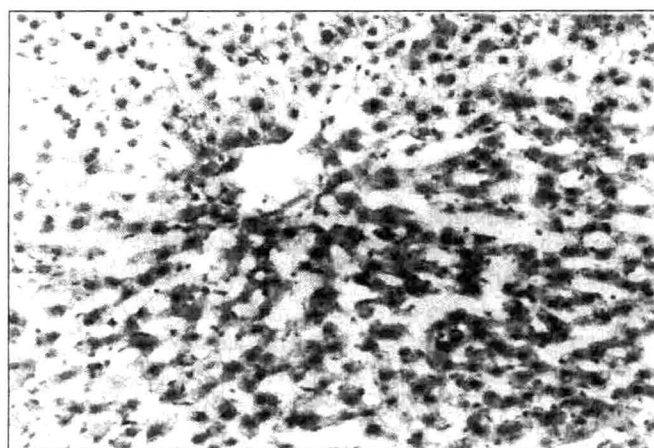
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serum was separated for estimating levels of marker enzymes such as glutamate oxaloacetate transaminase (GOT)¹⁸, glutamate pyruvate transaminase (GPT)¹⁸, alkaline phosphatase (ALP)¹⁹ and acid phosphatase (ACP)¹⁹. Immediately after sacrificing the animals, liver was rapidly excised, serially sectioned and microscopically examined. The tissue was fixed in 10% formalin and consecutive sections were stained with hemotoxylin and eosin. The data was analyzed using one way analysis of variance (ANOVA) followed by Dunnett 't' test. The level of significance was set at $P < 0.001$.

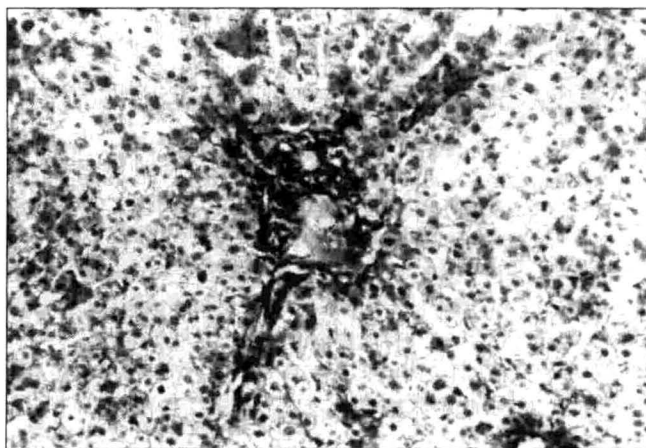
Oral administration of BG significantly decreased ($P < 0.001$) the elevated levels of SGPT, SGOT, ACP and ALP as compared to those found in CCl_4 -treated group. The levels

of serum marker enzymes were found to be elevated in CCl_4 -treated group as compared to the levels found in untreated controls as shown in Table 1. Fig. 1(a) exhibits the extensive loss of normal architectural structure of rat liver by CCl_4 treatment. The section showed extensive loss of hepatic lobules, centrilobular fatty degeneration, cloudy swelling and necrosis of hepatic cells. Fig. 1(b) exhibits the section of liver of rats treated with BG which showed normalcy of hepatic cells, central vein and portal triad.

CCl_4 is biotransformed by cytochrome P-450 system to produce the trichloromethyl free radical, which caused lipo-peroxidation²⁰. The administration of hepatotoxicant CCl_4 increases the serum levels of marker enzymes SGPT, SGOT, ACP and ALP indicating the induction of hepatotoxicity.



A



B

Fig. 1: Effect of *bramhi ghrita* treatment on ccl_4 -induced hepatic histopathological changes in rats.

1a shows liver of CCl_4 -treated rat. Section of liver showing centrilobular fatty degeneration, cloudy swelling and necrosis of hepatic cells. 1b shows the effect on *Bramhi Ghrita* (300 mg/kg) treated rat liver. Section of liver showing normalcy of hepatic cells.

TABLE 1: EFFECT OF *BRAMHI GHRITA* ON DIFFERENT BIOCHEMICAL PARAMETERS IN THE SERUM OF RATS

Treatment	SGOT units/ml	SGPT units/ml	Alkaline phosphatase ACP KA unit	Total acid phosphatase ACP KA unit
Control group	45.50±5.99	31.50±4.79	11.10±0.51	4.084±0.16
CCl_4	114.3±6.88*	126.3±6.88*	21.21±0.32*	12.25±0.53*
BG (100 mg/kg p.o.)+ CCl_4	85.50±12.27*	110.7±7.78*	18.91±0.35*	10.59±0.24*
BG (300 mg/kg p.o.)+ CCl_4	75.66±2.87*	82.50±4.27*	15.25±0.39*	7.61±0.46*

Values are mean±S.D., n=6, # $P < 0.001$ as compared with group I, * $P < 0.001$ as compared with group II, Statistical test employed is ANOVA followed by Dunnett 't' test.

Measurement of serum enzyme levels has provided a powerful tool for studies of hepatotoxicity²¹. Treatment with BG (100 mg/kg and 300 mg/kg) significantly prevented ($P < 0.001$) rise in the levels of SGPT, SGOT, ACP and ALP as compared with control group. The comparative histopathological studies of liver from different groups further corroborated the hepatoprotective efficacy of BG. On the basis of results obtained in the present investigation it can be concluded that BG exerts hepatoprotective activity and may serve as a useful adjuvant in several clinical conditions associated with liver damage.

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Surface Activity of Cox-2 inhibitors

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Surface tension of four cox-2 inhibitors, celecoxib, rofecoxib, meloxicam and nimesulide has been determined at 20°. Surface activity has been expressed in terms of surface pressure, surface excess and the area occupied on the liquid surface per drug molecule. Rofecoxib was not found to be surface active. Amongst other drugs, surface activity varied as nimesulide < meloxicam < celecoxib. Data was found to be in agreement with the octanol-water partition coefficients and polar surface area of drugs for all drugs except rofecoxib. Rofecoxib was exceptional in having small partition coefficient and small surface activity in spite of a very small polar surface area.

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