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Effect of *Bacopa monniera* on liver and kidney toxicity in chronic use of opioids

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Abstract

In the present study, we investigated the protective effect of *Bacopa monniera*, an indigenous Ayurvedic medicinal plant in India, against morphine-induced liver and kidney toxicity in rats. Morphine intoxicated rats received 10-160 mg/kg body weight of morphine hydrochloride intraperitoneally for 21 days. *Bacopa monniera* Extract (BME) pretreated rats were administered with *BME* (40 mg/kg) orally once a day 2 h before the injection of morphine for 21 days. Pretreatment with *BME* has shown to possess a significant protective effect against morphine-induced liver and kidney functions in terms of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase, lactate dehydrogenases and gamma-glutamyl transferase activities and urea, creatinine and uric acid level respectively. Histopathological changes of liver and kidney were also in accordance with the biochemical findings. The results of this study indicate that *Bacopa monniera extract* exerted a protection against morphine-induced liver and kidney toxicity.

Keywords: *Bacopa monniera*; Morphine; Liver toxicity; Kidney toxicity

Introduction

The central role of liver and kidney in drug metabolism predisposes them to toxic injury. Every drug has been associated with hepatotoxity almost certainly due to the pivotal role of the liver in drug metabolism. Hepatic metabolism is first, and foremost, a mechanism that converts drugs and other compounds into products that are more easily excreted and that usually have a lower pharmacologic activity than the potent compound (Tolman 1998). A metabolite may have higher activity and/or greater toxicity than the original drug. Metabolites of the drugs that are excreted from kidneys may also cause cellular damage leading to kidney dysfunction (Singhal et al. 1998).

Opiates have been used clinically for more than a century (Way 1979). Morphine, a classic synthetic opiate, is still the main stay of treating acute pain from surgery, angina, myocardial infarction, and trauma (Macpherson 2000). Morphine, which is commonly used for the treatment of severe pain, is metabolized essentially in the liver, gastrointestinal tract and kidney (Stain-Texier et al. 1998; Pacifici et al. 1986).

Bacopa monniera (Linn) Wettst (Syn.Herpestis monniera (Linn) H.B& K family scrophulariaceae is a medicinal plant commonly known as Brahmi, have been used in the indigenous systems of medicine for the treatment of various nervous systems ailments such as insomnia, anxiety, epilepsy, hysteria, etc. (Nadkarni 1976). Preclinical and clinical studies have shown that *Bacopa monniera* improves

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memory and mental function (Roodenrys et al. 2002). The chronic effects of an extract of *Bacopa monniera* on cognitive function in human subject have been reported (Stough et al. 2001). *Bacopa monniera* also exhibits potent antioxidant (Tripathi et al. 1996), anticancer (Elangovan et al. 1995), antiulcer (Sairam et al. 2001), calcium antagonist (Dar and Channa 1999), vasodilatory (Channa et al. 2003), mast cell stabilizing (Samiulla et al. 2001), anti-inflammatory (Jain et al. 1994), anti stress (Chowdhuri et al. 2002), inhibitory effect on *in vitro* morphine withdrawal in guinea pig ileum (Sumathi et al. 2002), and anti-addictive properties (Sumathi et al. 2007). The nootropic activity of the extract has been attributed to the presence of two saponins, namely *bacoside A* and *bacoside B*, of which the former is the more important (Singh and Dhawan 1997). The present study was designed to explore the protective effect of *Bacopa monniera* against morphine-induced liver and kidney toxicity in rats.

Materials and methods

Chemicals

Morphine hydrochloride used in the present study was obtained from Moti and company Ltd., Chennai, Tamil Nadu, India. All other reagents used were analytical grade, and obtained from Himedia, India.

Preparation of plant extract

The plant *Bacopa monniera* was collected in and around Chennai, India and authenticated by Dr. P. Brindha, Central Research Institute (Siddha), Chennai, India. The shade dried and coarsely powdered whole plant material (1 kg) was extracted with 90% ethanol in the room temperature (48 h). The extract was filtered and distilled on a water bath to obtain a dark green syrupy mass. It was finally dried in vacuo (yield 52 g).

Animals

Adult male albino rats of wistar strain (120–200 g) were used for the present study. They were acclimatized to the laboratory condition cycles and maintained under 12 h light/dark cycle at 25 ± 2 °C. The experiments were carried out in accordance with the guidelines provided by the Institutional Animal Ethical Committee.

Experimental design

Adult male albino rats of the Wistar strain weighing 200-250 g were maintained at constant temperature and light cycle with food and water ad libitum. After an acclimatization of 7 days, the rats were divided into four groups of six each. Group I rats received normal saline and served as a control. Group II, III and IV rats were treated with morphine hydrochloride, *BME* + morphine and *BME* alone respectively. While the dose of morphine hydrochloride was 10-160 mg/kg body weight/day i.p, for 21 days, that of *BME* was 40 mg/kg body weight/day orally 2 h before the administration of morphine hydrochloride. The experiment was carried out for 21 days. On the last day the animals were sacrificed by cervical decapitation. The blood samples were allowed to clot for 30-40 min, serum was separated by centrifugation at 3000 rpm for 15 min at 37 °C and used for various biochemical parameters.

HPLC-finger print analysis of *Bacopa monniera* extract

The following tabular column shows the exact data of the apparatus, column, solvent gradient, injection volume, detection wavelength and flow rate to which the *Bacopa monniera* extract was run for HPLC-finger print analysis.

HPLC system	: Shimadzu HT2010 Chromatographic system with in combination with Class LC 10A software & UV detection		
Column	: RP C-18 Luna phenomenex (250 × 4.6 mm)		
Column oven temperature	: 25 °C		
Mobile phase	: A-0.25% orthophosphoric acid in water		
	: B-Acetonitrile		
Flow rate	: 1.5 ml		
Injection volume	: 25.0 µl		
Gradient	: Time	A conc	B. conc
	: 0.00	75	25
	: 25.00	60	40
	: 35.00	40	60
	: 38.00	75	25.
	: 45	75.0	25
Detection wavelength	: 205 nm		
Run time	: 45 min		
Sample preparation	: Weigh accurately 500 mg extract to a 100 ml volumetric flask dissolve in 50 ml methanol, sonicate for 10–15 min. Cool then make up to 100 ml with methanol. Filter through 0.45 µm membrane filter paper		