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Therapeutic Potential Of Bacopa Monnieri Against Alcohol Induced Cardiac Toxicity In Rats

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Abstract

A study was conducted to investigate the potential protective effects of Bacopa monnieri extract on alcohol-induced toxicity in rats, focusing on its hypolipidemic and cardioprotective properties. For a period of 30 days, the experimental rats were orally intoxicated with alcohol (2 g/kg body weight) daily. Simultaneously, Bacopa monnieri extract was administered at a dose of 200 mg/kg body weight. The results of the study revealed that the rats subjected to alcohol-induced toxicity experienced a significant reduction in antioxidant defense systems, such as reduced glutathione (GSH) and ascorbic acid, while the activity of glutathione-S-transferase was enhanced compared to the control group. Additionally, the alcohol-induced group exhibited increased levels of triglycerides (TG) and total cholesterol (TC), as well as a significant decrease in phospholipids (PL). However, when Bacopa monnieri was supplemented along with alcohol, it significantly improved the antioxidant status and normalized the lipid profiles. These findings suggest that Bacopa monnieri possesses cardioprotective and hypolipidemic activities, which provide protection against alcohol-induced toxicity.

Key words: Alcohol, Bacopa monnieri, Glutathione, Ascorbic acid, lipid profiles

Introduction

Alcohol, which is found in alcoholic beverages, is a widely abused substance globally, excessive chronic alcohol consumption altered the lipid homeostasis, which could be caused to the development of cardiovascular disease (Walldius and Jungner., 2006). The primary cause of pathogenicity in alcoholic cardiac disease is the excessive production of reactive oxygen species (ROS), which leads to detrimental effects on the cellular antioxidant defense system (Ye et al., 2019). Additionally, it also contributes to the escalation of the lipid peroxidation process (Arulmozhi et al., 2010).

Alcohol and its metabolites can cause mild to severe tissue injuries, mainly due to impaired antioxidant status and oxidative stress (Mallikarjuna et al., 2010). This, in turn, causes a destructive process called lipid peroxidation, leading to the progressive degradation of cell membranes. As a result, both the integrity of cell membranes within the cells and those surrounding them are compromised, severely impacting cellular function. Continuous and excessive alcohol consumption can accelerate oxidative mechanisms, either directly or indirectly, leading to tissue damage and ultimately, cell death (Lieber et al., 2000). Previous research has demonstrated that the consumption of alcohol leads to modifications in the different lipid components present in the livers of humans and animals. These lipid abnormalities that arise following alcohol intake encompass variations in triglyceride levels, cholesterol levels, fatty acid levels, and notably, changes in the fatty acid composition of membrane phospholipids (Semenkovich et al., 2011).
According to a study conducted by Zhou et al. (2003), antioxidants derived from plants have been found to have the potential to hinder or stop the occurrence of underlying cellular imbalances caused by excessive alcohol consumption. In a recent study conducted on rats, researchers aimed to assess the potential cardioprotective effects of Bacopa monnieri, commonly known as Brahmi, against chronic alcohol consumption. Brahmi contains various bioactive compounds such as saponins, alkaloids, triterpenes, flavonoids, and cucurbitacin, which are believed to possess antioxidant properties. The study focused on examining the impact of Brahmi on the lipid profile and antioxidant status in the heart of rats subjected to prolonged alcohol administration.

Materials and Methods

Animals

In the present study, a group of thirty male albino rats (Wistar strain) weighing 180 ± 20 g each were utilized. These rats were maintained on a standard pellet diet and had unlimited access to water. They were housed in polypropylene cages under controlled conditions, with a temperature of 25.6 ± 28oC and a 12-hour light/12-hour dark cycle.

Chemicals

we used all the chemicals used were Analar Grade (AR) and attained from the the following reputable scientific companies: Fischer (Pitrsburg, PA, USA), Sigma (St. Louis, MO, USA), Merck (Mumbai India), and Qualigens (Mumbai, India) and Ranbaxy (New Delhi, India),

Preparation of plant extract

The Bacopa monnieri leaves used in this study were sourced from plants cultivated in pots within the premises of Sri Venkateshwara University campus. A thorough washing process was implemented, ensuring that any dirt or soil particles attached to the leaves were eliminated using running tap water. Subsequently, the leaves were carefully dried using tissue paper to remove any remaining water droplets. Fresh leaves of Bacopa monnieri were carefully collected and processed to prepare a methanolic extract with a final concentration of 200 mg/ml. After evaporating the methanol, the remaining extract was dissolved in water to facilitate gavage feeding.

Experimental design

Thirty rats divided into five groups of six rats in each group and treated as follows:

1. Normal control (NC): For a duration of 30 days, this particular rat group was administered saline solution (0.9%).
2. Alcohol treatment (At): This group of rats received absolute alcohol orally with 2 g/kg body weight via orogastric tube for thirty days.
3. Bacopa monnieri treatment (Bt): Rats treated with Bacopa monnieri extract (200mg/kg body weight.
4. Alcohol treatment + Bacopa treatment (At+Bt): This group of rats received both alcohol and Bacopa monnieri as described in group 2 and group 4 for Six weeks.

Tissue collection and Analytical procedures

After a duration of twenty-four hours, the animals were euthanized by cervical dislocation for the final treatment. The heart was carefully removed at a temperature of 4°C, washed with ice-cold saline solution, and gently dried. Subsequently, the heart tissue, with atria and blood vessels properly trimmed, was promptly submerged in liquid nitrogen for preservation at -80ºC for future biochemical analysis. To assess specific lipid metabolic profiles like phospholipids (PL), triglycerides (TG), and total cholesterol (TC), the methods outlined

by Zilversmidth and Davis (1950) and the Liebermann Bernhard reaction described by Natelson (1971) were employed, respectively. The measurement of ascorbic acid levels, as well as the determination of GSH (glutathione) and GST (glutathione S-transferase) activity, followed the protocols established by Omaye et al. (1971) and Theodorus et al. (1981). It is important to note that all experiments conformed strictly to the guidelines and protocols approved by the Institutional Animal Ethics Committee.

Statistical analysis:

The results expressed were expressed as means six rats per group for control and experimental animals. The data were analysed using one-way analysis of variance (ANOVA) on SPSS/PC and the group means were compared by Duncan's Multiple Range Test (DMRT). The results were statistically considered significant the P value was less than 0.001.

Results

In the current study, alcohol-treated rats exhibited a notable reduction in GSH, Ascorbic acid, and enhanced GST activity (Table 1). However, administration of Bacopa monnieri had a restorative effect and returned these parameters to their normal levels. This suggests that Bacopa monnieri treatment effectively normalized the heart antioxidant enzyme levels that had been altered due to alcohol consumption.
The heart lipid profile in both control and experimental animals was analysed and the findings are presented in Tables 2. The results indicate that the levels of total cholesterol, triglycerides, and phospholipids showed a significant increase in rats exposed to alcohol. However, when Bacopa monnieri was co-administered, the lipid profile gradually improved and approached normal levels.

Discussion

Oxidative stress is an imbalance between the amount of intracellular ROS and antioxidant defense status. Alcohol intoxication is characterized by elevated oxidative stress and decreased antioxidant enzyme status in various tissues, including liver and heart of rodents (Dai et al., 2021). In the current study, we observed GSH was decreased in alcohol treated rat group. in the heart, a decrease in enzyme activities associated with the utilization and recycling of glutathione as a result of prolonged alcohol exposure (Kode et al., 2004). According to earlier research, it has been found that the level of glutathione was reduced in the liver tissue of rats that were exposed to alcohol (Rodrigo et al.,2002). Alcohol consumption triggers the process of lipid peroxidation and decreases the levels of Glutathione (GSH), an important antioxidant. As alcohol is metabolized, it generates metabolites that further contribute to the oxidation of GSH through the production of reactive oxygen species (ROS) intermediates, as observed in a study by Bilanda et al. in 2004. Consequently, the GSH concentration decreases as a result of this metabolic activity. According to previous research (Ahmad et al 2000), it has been observed that rats treated with Bacopa monnieri showed an increase in GSH levels after consuming alcohol. These findings suggest that Bacopa monnieri may have an antioxidant effect, as it is believed to decrease lipid peroxidation, elevate GSH levels, and help maintain the normal functioning of antioxidant enzymes. Treatment of Bacopa monnieri extract showed protective effect in alcohol rats by enhancing the antioxidant enzyme activities including GSH level.
The increased involvement of glutathione in the conjugation process, facilitated by the elevated activity of GST, seems to offer a plausible explanation for the reduced levels of GSH observed after alcohol consumption (Dinu et al., 2005). Das and Vasudevan (2005) noted in their dose-dependent alcohol studies that increased GST activity indicates its activation in response to oxidative stress. Feeding Bacopa monnieri has been shown to stimulate GST in cardiac tissue, suggesting that it may offer protection against the harmful effects of xenobiotics. The rise in GST activity in cardiac tissue provides additional evidence for the theory that consistent consumption of Bacopa monnieri can boost the performance of phase II detoxification enzymes.
As a scavenger of ROS (Reactive Oxygen Species), ascorbate has shown to be effective in neutralizing the superoxide anion radical, hydrogen peroxide, the hydroxyl radical, and singlet oxygen. In our study, we observed a decline in heart ascorbic acid levels specifically in the alcohol-treated group. This drop may be linked to the increased use of this antioxidant to combat the free radicals generated during acute alcohol intoxication (Balasubramanian et al., 2003). In the current study with bacopa monnieri treatment in alcohol treated group, ascorbic acid level was increased. This could be attributed to the impact of flavonoids and bacosides, compounds present in Bacopa, on Reactive Oxygen Species (ROS) generated during alcohol

metabolism. Consequently, Bacopa monnieri might have a potential therapeutic effect in neutralizing harmful free radicals in the cardiac tissue.

The consumption of alcohol is known to promote the synthesis of fatty acids and cholesterol, while simultaneously reducing their breakdown. This can lead to elevated levels of triglycerides (hypertriglyceridemia) and cholesterol (hypercholesterolemia) (Kumar et al., 2002). Previous studies confirmed that chronic alcohol feeding could rise the lipolytic activity and elevate Free fatty acids concentration. The increased FFAs with alcohol consumption may rise the circulating triglycerides concentrations, which may be due to enhanced phosphatide phosphohydrolase activity (Yao et al., 2020). Increased Triglycerides levels after alcohol absorption may be due to the increased availability of glycerophosphates, free fatty acids decreased Triglycerides lipase activity, and decreased fatty oxidation. These increased TG levels may lead to increased accessibility of Free fatty acids for esterification. Phospholipids are the vivacious components of a bio membrane and mainly act as membrane-bound enzymes regulators important in influential the alcoholism pathology. (Thoen et al., 2023). Hence, the alteration in the membrane composition may be the reason for the toxic defects caused by alcohol. The decreased phospholipid levels in the heart may be due to the increased activity of phospholipases in the cardiac tissue. Earlier studies have demonstrated that chronic exposure to ethanol may lead to a progressive increase in membrane phospholipase activity (Kim et al., 2012). Hence, the alteration in the membrane composition may be the reason for the toxic defects caused by alcohol. Thus, the Bacopa monnieri extract consumption could result in accumulation of active ingredients within the cells, as well as in the cell plasma membrane receptors may reduce the plasma TG by increasing pancreatic lipase and amylase, which inhibit lipid hydrolyse in intestinal tract reducing lipid peroxidase (Liu et al., 2003). The pretreatment of Bacopa monnieri extract was active in counteracting the oxidative stress induced damage by decreasing the cardiac lipid levels of rats. The significant increase levels of cholesterol, phospholipids triglycerides, and free fatty acids in the heart caused by the administration of streptozotocin in rats were brought down to normalcy on treatment with Bacopa monnieri.

Conclusion:

The findings indicate that alcohol treatment elevated lipid metabolic profiles and reduced antioxidant status. However, the administration of Bacopa monnieri extract resulted in a significant decrease in lipid profile activities, suggesting its protective effect, without any observed toxic effects. Similarly, the antioxidants also showed similar trends. These results provide evidence of the Cardioprotective properties of Bacopa monnieri extract against alcohol-induced cardiac toxicity.

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Table. 1 Effect of Bacopa monnieri extract on glutathione (GSH), Ascorbic acid (AA) and Glutathione -S-transferase (GST) in rats with alcohol induced oxidative stress in rat heart.

Groups	GSH (µmol of uric acid/ g wet weight of the tissue)	Ascorbic acid (mg ascorbic acid / wet weight of tissue	GST (µmol of glutathione / mg protein/min)
Normal control (NC)	11.214±0.286	0.476±0.020	26.74±0.041
Alcohol treated (At)	8.256±0.345* (−27.785)	0.247±0.034* (−24.594)	43.864±0.028* (−53.31)
Bacopa treated (Bt)	11.574±.896* (+42.467)	0.489±0.102* (+46.355)	26.56±0.074* (+64.712)
Alcohol plus Bacopa (At+Bt)	10.123±0.483** (+11.398)	0.394±0.018** (+31.294)	37.542±0.186** (+42.356)

All the values are mean±SD of six individual observations.
Values in the parenthesis denote percent change over normal control.
The values are significant compared to the following: control (*p < 0.001),
alcohol treated (** < 0.01) (Dunnett's multiple comparison test).

Table 2. Effect of Bacopa monnieri on cardiac lipid profiles in control and alcohol-administered rats

Groups	Triglycerides mg/g of tissue	Phospholipids mg/g of tissue	Total cholesterol mg/g of tissue
Normal control (NC)	5.12 ± 5.15	19.54 ± 3.98	4.21±1.99
Alcohol treated (At)	9.32± 4.94* (+13.256)	14.51 ±10.17* (+33.214)	8.14.6±7.55* (+54.124)
Bacopa treated (Bt)	5.42±1.456* (-44.056)	19.09±1.658* (-54.742)	4.20±2.456* (−21.518)
Alcohol plus Bacopa (At+Bt)	6.32 ± 6.21** (+21.148)	17.65 ± 4.19** (+20.245)	6.97±7.56** (+38+.874)

All the values are mean±SD of six individual observations.
Values in the parenthesis denote percent change over normal control.
The values are significant compared to the following: control (*p < 0.001),
Alcohol treated (** < 0.01) (Dunnett's multiple comparison test).