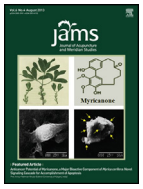
Available online at www.sciencedirect.com

Journal of Acupuncture and Meridian Studies

journal homepage: www.jams-kpi.com



RESEARCH ARTICLE

Evaluation of *Bacopa monniera* for its Synergistic Activity with Rivastigmine in Reversing Aluminum-Induced Memory Loss and Learning Deficit in Rats

Agadi Hiremath Thippeswamy, Mohamed Rafiq*,
Gollapalle Lakshminarayana shastry Viswantha, Kethaganahalli J. Kavya,
Suryakanth D. Anturlikar, Pralhad S. Patki

Department of Pharmacology, R&D Center, The Himalaya Drug Company, Makali, Karnataka, India

Available online Mar 22, 2013

Received: Dec 4, 2012
Revised: Feb 1, 2013
Accepted: Feb 13, 2013

KEYWORDS
aluminum chloride;
Bacopa monniera;
elevated plus maze;
memory impairment;
Morris water maze;
rivastigmine

Abstract
The objective of this study was to evaluate the synergistic activity of *Bacopa monniera* with Rivastigmine against aluminum-chloride ($AlCl_3$)-induced cognitive impairment in rats. Adult male Wistar rats were divided into ten groups (n = 10) and subjected to their assigned treatments for 42 days. On the 20th day of the respective drug treatments, all the animals were trained in the Morris water maze (retention latency) and the elevated plus maze (transfer latency). After the initial training, the retention latency (RL) and the transfer latency (TL) were evaluated on the 21st and the 42nd days of the study. Chronic administration of $AlCl_3$ caused significant memory impairment associated with increased RL in the Morris water maze task and increased TL in the elevated plus maze test. Interestingly, animals treated with oral administration of *B. monniera* (100 and 200 mg/kg), Rivastigmine (5 mg/kg) or a combination of *B. monniera* (100 mg/kg) with Rivastigmine (5 mg/kg) showed significant protection against $AlCl_3$-induced memory impairment compared to animal treated with $AlCl_3$ *per se*. Additionally, the neuroprotective effect of *B. monniera* (100 and 200 mg/kg) was significantly improved when supplemented with Rivastigmine (5 mg/kg). These findings suggest that treatment with a combination of *B. monniera* with Rivastigmine may be highly beneficial compared to their *per-se* treatment.

* Corresponding author. Department of Pharmacology, R&D Center, The Himalaya Drug Company, Makali, Bangalore 562 123, Karnataka, India.
E-mail: dr.rafiq@himalayahealthcare.com

pISSN 2005-2901 eISSN 2093-8152
http://dx.doi.org/10.1016/j.jams.2013.02.004

1. Introduction

Developing effective and safe therapeutic treatment strategies for cognitive disorders, such as amnesia, attention deficit hyperactivity disorder, and Alzheimer's disease (AD), remains a challenge in the field of medicine [1]. The pathological hallmarks of cognitive disorders are memory loss and learning deficits. Environmental factors have been suggested as one of the possible contributory causes to the development of neurological disorders [2]. In this context, long-term consumption/exposure to aluminum is also thought to be a causative factor in the pathogenesis of AD [3]. Exposure to aluminum is not usually harmful and is not inherently toxic. However, a high concentration of aluminum is found in people with Parkinson's disease, senile dementia, amyotrophic lateral sclerosis, and senile dementia associated with AD [4].

Aluminum is a well-known neurotoxicant reported to accelerate oxidative damage to biomolecules. It crosses the blood—brain barrier through the high affinity transferrin receptors [5] and: (1) causes protein misfolding; (2) causes self-aggregation of highly phosphorylated cytoskeletal proteins, such as neurofilaments, microtubule-associated proteins, and amyloid-β; and (3) inhibits slow and fast axonal transports by damaging synaptic architecture, and induces neuroinflammation [6]. Additionally, aluminum is a potent cholinotoxin that causes apoptotic neuronal loss and also impairs hippocampal long-term potentiation. All these neurological perturbances ultimately result in learning and memory deficits in animals and humans. Further, aluminum has been reported to be found in both senile plaques and neurofibrillary tangle-bearing neurons in the brains of patients with AD [7].

In the context of treating cognition and related disorders, plant-based medicines have been used in folk medicine. Some medicinal plants have been scientifically proven to possess potent cognition-enhancing properties [8,9]. *Bacopa monniera* of the family Scrophulariaceae is a well known cognitive enhancer in the Indian system of traditional medicine [10]. It is also referred to as *Herpestis monniera* and is commonly called Brahmi [11]. *B. monniera* was traditionally used as a brain (nerve) tonic to enhance memory, learning, and concentration. It has been scientifically proven to possess anti-inflammatory [12], analgesic [13], antipyretic [14], sedative [15], antiepileptic [16], anxiolytic [14], antidepressant [17], and antioxidant properties [18].

Studies have reported that *B. monniera* has anticholinesterase activity (aids learning and memory skills), and adaptogenic and antidepressant activity in both acute and chronic stress situations [19]. It has also been shown to be beneficial in reversing scopolamine-induced oxidative stress and dementia in experimental animals [10,14,19]. In light of this, the present study was conducted to evaluate the possible synergistic activity of *B. monniera* with rivastigmine in reversing $AlCl_3$-induced learning deficits and memory loss in rats.

2. Materials and methods

2.1. Animals

Inbred adult male albino Wistar rats (180—200 g body weight) were used for the study. Animals were housed in standard isolation cages under standard environmental conditions with a temperature of 22 ± 2°C, relative humidity of 60 ± 5% and a 12 hour light—dark cycle. Rats were allowed free access to water and standard laboratory rat chow (Provimi Animal Nutrition India Pvt Ltd, Bangalore, India).

2.2. Ethics approval

All the experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) of The Himalaya Drug Company and were conducted according to the guidelines of the Committee for the Purpose of Control and Supervision of Experimentation on Animals (CPCSEA), India.

2.3. Chemicals and reagents

B. monniera (Bacopa) granules (The Himalaya Drug Company, Bangalore, India) and rivastigmine (Sun Pharmaceuticals Ltd, Mumbai, India) were used for the study; all other chemicals and reagents were of analytical grade (HiMedia Laboratories Pvt Ltd, Mumbai, India).

2.4. Experimental protocol

One hundred male Wistar albino rats were randomized into 10 groups (G1—G10), each with 10 animals. The animals in G1 were treated with vehicle and served as controls. Animals in G2 and G7 were treated with 5 mg/kg rivastigmine p.o., G3 and G8 with 100 mg/kg *B. monniera* p.o., G4 and G9 with 200 mg/kg *B. monniera* p.o., and G5 and G10 with a combination of 5 mg/kg rivastigmine and 100 mg/kg *B. monniera* p.o. Along with their assigned drug treatments, the animals in G7, G8, G9, and G10 were challenged with $AlCl_3$ (100 mg/kg p.o.) daily for 42 days to induce learning deficits and amnesia; animals in G6 served as positive controls and only received $AlCl_3$.

A flow chart of the experimental protocol is shown in Fig. 1.

2.5. Assessment of cognitive parameters by the Morris water maze test

Animals were trained to swim to a visible platform in a circular pool (180 cm in diameter and 60 cm in height) located in a test room. In principle, rats can escape from swimming by climbing onto the platform and over time the rats apparently learn the spatial location of the platform from any starting position at the circumference of the pool. The pool was divided into four equal quadrants and filled with water to a height of 40 cm. During the acquisition phase, a movable circular platform (9 cm diameter) was placed in one of the quadrants of the pool approximately 2 cm above the water level, and during the retention phase, a similar platform was placed in the pool 2 cm below the water level. The water was made opaque by adding a nontoxic dye and four locations were equally spaced around the edge of the pool (N, S, E, and W) and used as starting points for the acquisition phase [4,20].