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ORIGINAL ARTICLE

Black seed oil ameliorated scopolamine-induced memory dysfunction and cortico-hippocampal neural alterations in male Wistar rats

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Abstract This study was conducted to evaluate cognitive enhancing effect and ameliorative effects of black seed oil in scopolamine induced rat model of cognitive impairment. These effects were investigated on scopolamine-induced dementia model in Morris water maze test (MWM) and Y maze test. The hippocampal histoarchitectural responses to scopolamine and *Nigella sativa* oil were also examined.

Scopolamine (1 mg/kg ip) was given to induce dementia, followed by oral administration of BSO (1 ml/kg) for 14 consecutive days. MWM and Y-maze paradigms were used to assess hippocampal and frontal dependent memory respectively, thereafter the rats were sacrificed and brains were removed for histopathologic studies.

Scopolamine resulted in memory impairment, by delayed latency in the MWM, reduced percentage alternation in the Y maze that was coupled by alterations in the cortico-hippocampal neurons. Post-treatment of rats with BSO mitigated scopolamine-induced amnesia, by reducing latency period and increasing percentage alternation and histological changes. The observed anti-amnestic effect of BSO makes it a promising anti-amnesic agent for clinical trials in patients with cognitive impairment.

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1. Introduction

Dementia is characterized by a loss or decline in memory and other cognitive functions, and one of the most common sub-

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types of dementia is Alzheimer's disease (AD).[1] AD is characterized by a cascade of conditions like neural oxidative stress, deposition of amyloid plaques, neurofibrillary tangles, inflammation and impaired central functions.[2] The implicated mechanism of AD in the elderly sufferers is linked to the loss of cholinergic neurons in the basal forebrain and hippocampus.[3]

Scopolamine is a muscarinic receptor antagonist with profound amnesic effects in a variety of learning paradigms and a useful experimental pharmacological model to investigate the pathophysiology of the cognitive deficit in AD.[4] It has been widely implicated to cause amnesia and a viable model of dementia in humans and animals.[5–7] Scopolamine caused its cholinergic deficits via oxidative stress[8,9] and neuroinflammation.[10] Scopolamine induced memory deficits have been widely implicated for the screening of anti-dementia drugs.[11,12]

The most common treatment modalities for AD symptoms are the cholinesterase inhibitors, whose primary targets are AChE and BChE for their therapeutic activities. However, these agents cause undesirable side effects, thereby limiting their use. The present therapies produce modest symptomatic improvements in patients; thus, searching for alternative or supplement anti-amnesic agent is an ultimate necessity.

Herbal and natural plant extracts have gained wide attention in their use in the treatment and/or management of neurological, psychiatric and degenerative diseases, due to their no or less side-effects.[13,14] Black seed oil is a high value medicinal solvent, widely used traditionally in the treatment of many diseases. Compelling evidences have reported that black seed oil (BSO) exhibits protective activities against many diseases depending on its high antioxidant[15] and anti-inflammatory properties.[16] This could suggest its use as a potential remedy for cognitive impairments in AD.

A number of studies have been carried out, acclaimed medicinal properties emphasized on different pharmacotherapeutical efficacies of black seed oil such as antioxidative[17] and neuroprotective,[15,18] antiasthmatic,[19] anti-inflammatory, immunomodulatory and anti-tumor properties,[16] gastric ulcer healing,[20] tumor growth suppression,[21] men infertility improvement,[22] and stimulate milk production.[23] The main active ingredients in BSO are thymoquinone (TQ), alkaloids (nigellidine, nigellimine, and nigellicine), vitamins such as thiamine, riboflavin, pyridoxine, niacin, and folic acid, minerals, and proteins.[24]

The present study was designed to investigate the ameliorative efficacy of BSO against behavioral alterations in scopolamine demented rats. Their neuroprotective effects on cortico-hippocampal neuronal alterations were also evaluated.

2. Materials and methods

2.1. Drugs

Scopolamine hydrobromide (sigma, USA) was used in the present study. Scopolamine was dissolved in saline (NaCl 0.9%) at final concentrations of 1 mg/kg, and was injected intraperitoneally. The black seed oil (100% pure natural oil) was obtained from Masra warda, Kingdom of Saud.

2.2. Experimental animals

Eighteen adult albino Wistar rats weighting 200 ± 20 g at the time of acquisition and acclimatization were used in this study. They were housed singly in metabolic cages under standard laboratory conditions in Animal holding of the Faculty of Basic Medical Sciences, University of Ilorin, Ilorin. They had free access to food and water, were housed six in a cage, and kept at controlled temperature (22 ± 2 °C) under a 12/12 h light-dark cycle. All procedures were performed in accordance with institutional guidelines for animal care and use.

2.3. Treatments schedule

The rats were randomly distributed into four groups ($n = 6$) as follows:

A. received saline for 14 days
B. received BSO (1 ml/kg) orally for 14 days
C. received scopolamine (1 mg/kg) intraperitoneally for 14 days
D. BSO (1 ml/kg) orally, 30 min after scopolamine (1 mg/kg) intraperitoneally for 14 days

All experiments were carried out during the light phase between 9:00 and 15:00. Experimental groups consisted of 6 animals each.

2.4. Ethical approval

All procedures were performed in accordance with institutional guidelines for animal care and use and ethical approvals were received the University of Ilorin ethics review committee.

2.5. Morris water maze test

Morris water maze is one of the most widely used tasks for testing spatial learning and memory in rodents and the procedure used in the present experiment was a modification. In this test, water maze consists of a circular pool (1.6 m diameter and 50 cm height) colored with black nontoxic dye filled to a depth of 44 cm with water. The temperature in pool was maintained at 25 ± 1 °C. Four equally spaced points around the edge of the pool were designed as North (N), East (E), South (S) and West (W). A black colored round platform of 9 cm diameter was placed 1 cm below the surface of water. The rats were trained to navigate the submerged platform. The rats were given a maximum time of 120 s (cut-off time) to find the hidden platform and were allowed to stay on it for 30 s. The platform remained in the same position during the training days. Rats that failed to locate the platform within 120 s were put on the platform only in the first session. The animals were given a daily session of five trials. Escape latency time to reach the platform was recorded in each trial.

2.6. Y maze

The behavioral test was conducted in a large quite room. Y-maze apparatus was used to assess the animals' spatial memory. A stop watch was used to score the behaviors and all events were observed manually. A Y-maze is made up of three equally spaced arms, labeled as A, B, and C which are 120° from each other, 41 cm long and 15 cm high. It was used to assess the spontaneous alternation in the rats. The floor of