PROTECTIVE EFFECT OF SR-105, AGAINST NaNO₂ INDUCED HEMIC HYPOXIA

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Abstract

The present study was undertaken to study the effect of SR-105, against sodium nitrite induced hemic hypoxia in experimental animals. Sodium nitrite induces chemical hypoxia by reducing oxygen-carrying capacity of the blood with converting hemoglobin to methaemoglobin causes hemic hypoxia. The various dose of SR-105(100, 200, 400, 600 & 1000 mg/kg bw), a polyherbal formulation was administered in mice. The dose dependent activity of SR-105 shows protection against sodium nitrite induced hemic hypoxia. Simillarly effect of piracetam also evaluated. Apart from central neurotransmitters, cognitive deficits induced by impairment of cerebral metabolism and cerebral blood flow. And it is proposed that improvement of cerebral metabolism and blood flow beneficial to learning and memory. The SR-105, reverse the cognitive deficits induced by hypoxia comparable with Piracetam. However the SR-105 may be worthwhile to explore the potential of this formulation in the management of Alzheimer patients.

Key words: SR-105, Piracetam, Alheimer’s disease, Hemic Hypoxia.

1. INTRODUCTION

Sodium nitrite is a common meat preservative and dye that has both harmful and healthful effects. Check packages of processed meats, such as bacon, hot dogs, sausage and sliced deli meats, and chances are you'll find the term on the ingredients list. Sodium nitrite is sometimes used for medicinal purposes, and it might one day be used as part of the treatment for heart attack and sickle-cell anemia patients[1,2]. However, under certain conditions, sodium nitrite can break down into another substance known to cause cancer, Alzheimer's disease and fatty liver disease [3]. Alzheimer’s disease (AD), as the most common form of progressive dementia, is characterized neuropathologically by the presence of intracellular neurofibrillary tangles and features resulting from the deposition of amyloid β-peptide (Aβ) extracellularly in the form of senile plaques and within blood vessels in the brain in the form of cerebral amyloid angiopathy[4]. AD has been identified as a protein misreading disease due to the accumulation of abnormally folded amyloid beta protein in the brains of AD patients[5,6]. In AD patients, hyperphosrylated tau accumulates as paired helical filaments[6,7], that in turn aggregates into masses inside nerve cell bodies known as neurofibrillary tangles.
Recently, several in vitro studies have shown a role played by oxygen-free radicals in promoting amyloid aggregation, as well as the protective effects of some free-radical scavengers, such as vitamin E, an natural antioxidant traps free radicals, may inhibit lipid peroxidation and delayed AD[8]. Considering the available literature in ayurveda, we and SHRUSHTI a Herbal Pharma Industry of Bangalore had planned to study the effect of SR-105, polyherbal formulation against sodium nitrite induced hemic hypoxia in experimental animals.

2. MATERIALS AND METHODS

2.1 Drug and Chemicals
Piracetam(200mg/kg) (‘Neurocetam syrup’, Brown & Burk.India) used as standard drug, Sodium Nitrite (Ranbaxy Lab Ltd India) and SR-105 (SHRUSHTI a Herbal Pharma Industry of Bangalore) in the form of tablets. SR-105 is a polyherbal formulation contains Convolvulus microphyllus, Cellastrus paniculata, Acrorus calamus and Bacopa monniera. All drugs were dissolved in distilled water and administered orally.

2.2 Determination of Acute Toxicity (LD50)
The LD50 studies of SR-105 were calculated according to OECD guidelines No.425 by using albino mice of either sex (20-30 g) and there is no mortality during 48 h study period. LD50 of polyherbal formulation SR-105 is more than of 2000 mg/kg.

2.3 Animals
Animal studies were performed as per rules and regulations in accordance to guideline of CPCSEA with registration number 557/02/c/CPCSEA,18.2.2002. The SR-105 with different doses was administered for 14 days to experimental animal for evaluation of protection against hemic hypoxia. Group of adult Swiss male albino mice 18-25g, each consisting of 6 animals was divided into following groups and animals are fasted overnight prior to the test but water was supplied ad libitum.

2.4 Treatment Schedule
Group I was maintained as normal control which was given with distilled water (10ml/kg, p.o.), Group II with Sodium nitrite alone (250 mg/ kg s.c) daily once for 14 days Group III with piracetam (200 mg/kg, p.o.) which served as standard, Groups IV, V, VI VII and VIII were treated with different doses of SR-105 (100,200,400,600 and 1000 mg/kg p.o.) a polyherbal formulation respectively daily once for 14 days as mentioned above.

2.5 Induction of Chemical Hypoxia
All the groups was treated according to the protocol for a period of 14 days and sodium nitrite 250mg/kg was given s.cly 60 minutes after last dose of standard/ polyherbal formulation to induce chemical hypoxia. Sodium nitrite reduces the oxygen carrying capacity of the blood by converting hemoglobin to methemoglobin and cessation of respiration time in each group was recorded [9].

3. RESULTS
3.1 Effect of SR-105 on sodium nitrite intoxication model in mice
Sodium nitrite treated group had shown 13.09±0.7374 min for cessation of respiration. Prior treatment with piracetam and different doses of SR-105 had showed increased the time for cessation of respiration. However, a significant effect was observed with piracetam and different doses of SR-105 as compared sodium nitrite alone treated group (Table 3.1). SR-105 had been shows dose dependent protection, as the dose increases the protection also increases as compared to piracetam treated group (Fig 3.1).

4. DISCUSSION
Nootropics, popularly referred to as “smart drugs”, are substances, which boost human cognitive abilities (the functions and capacities of the brain). Typically these are thought to work by increasing the brain’s supply of neurochemicals (neurotransmitters, enzymes and hormones) improving brain’s oxygen supply or by stimulating nerve growth [10]. The American Medical Association reports that
consumption of large quantities of nitrates leads to formation of methemoglobin, which means oxidized hemoglobin. In the oxidized form, hemoglobin can't carry oxygen to the tissues, leading to tissue oxygen starvation. Sodium nitrite impaired memory was through the cholinergic innervations i.e. it causes hypoxia leading to decreased oxygen content in the brain as suggested by Koziar et al[11]. The sodium nitrite produces hemic hypoxia i.e. which reduces the oxygen-carrying capability of the blood by converting hemoglobin to methemoglobin. The protective effect existing by polyherbal formulation SR-105 (100, 200, 400, 600 and 1000mg/kg) and piracetam (200mg/kg) against sodium-nitrite-induced hemic hypoxia model may be due to enhanced brain metabolism by increased oxygen content in brain.

5. CONCLUSION
In the light of above, it may be worthwhile to explore the potential of this polyherbal formulation SR-105 useful in management of Alzheimer’s disease.

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7. REFERENCE


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