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RESEARCH ARTICLE

AN EXPERIMENTAL STUDY TO EVALUATE THE EFFECT OF *MUCUNA PRURIENS* ON LEARNING AND MEMORY IN MICE

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ABSTRACT

Introduction: Nootropics, popularly referred to as smart drugs, smart nutrients, cognitive enhancers, brain enhancers and memory enhancers are a class of drugs that improve impaired human cognitive abilities. *Mucuna pruriens*, belonging to family Fabaceae, has been used in traditional Ayurvedic medicine for various ailments. Present study was undertaken to evaluate the cognitive enhancer activity of acute and chronic administration of *Mucuna pruriens* in Y maze.
Methods: The study was conducted on 30 male Swiss albino mice. Animals were divided into five groups (n = 6 /group): control group (normal saline, p.o.), standard group (Piracetam, 30mg/kg, i.p.) andthree doses of *Mucuna pruriens*(100, 200, 400 mg/kg, p.o.) for 14 days treatment. Assessment of Spontaneous Alteration Behaviour and total number of entries in different arms using the Y- maze acts as a validated model for measuring learning and memory activity.
Results: MPE has shown dose dependent increase SAB on day 7 & day 14. Among the groups which received different doses of MPE, the maximum % alteration rate is seen at dose of 400mg/kg. There is decrease in number of entries from day 7 to day 14 in all the test drugs groups. Highest decrease is seen with MPE in a dose of 400mg/kg which is almost similar to decrease in standard group (Piracetam).
Conclusions: This study demonstrated the cognitive enhancer activity (memory, learning etc.) of *Mucuna pruriens* in Swiss albino mice. The cognitive enhancer activity of *Mucuna pruriens* was comparable to that of standard drug, piracetam.

Key Words: *Mucuna pruriens,* Y maze, learning, memory, Piracetam.

INTRODUCTION

Learning is defined as the process of acquiring new information or skills, whereas memory refers to the persistence of learning that can be revealed at a later time (Parle *et al*., 2004; Squire *et al*., 1987). Memory is the usual consequence of learning and reflects the enduring changes in the nervous system that result from transient experiences. Poor Memory, lower retention and slow recall and are common problems in today's stressful and competitive world. Age, stress, emotions are conditions that may led to memory loss, amnesia, anxiety, high blood pressure, dementia, to more ominous threat like schizophrenia and Alzheimer's diseases and in that case the person is not able to make full use of his or her potentials. Among the neurotransmitters involved in learning and memory processes, acetylcholine (ACh) is the well-known neurotransmitter of the basal fore-brain cholinergic neurons that is associated with cognitive processes, including sensory stimulus processing, alertness, aurosal and memory function (Auld *et al*., 2002). Stress can alter cognition by modulating both norepinephrine (NE) and cortisol activity (Skosnik *et al*., 2000). NE-depletion in rodents and monkeys was shown to cause increased distractibility and deficits in spatial working memory, while administration of NE agonists improved memory performance (Arnsten *et al*., 1992; Arnsten *et al*., 1991; Arnsten *et al*., 1988; Carli *et al*., 1983; Brozoski *et al*., 1979; Roberts *et al*., 1976). Other transmitter systems, such as the dopaminergic, and serotonergic system, are also involved in learning and memory processes (Blokland *et al*., 1995; Myhrer 2003; Robbins *et al*., 1998). The serotonergic system is believed to be especially relevant in mediating the acquisition processes in memory formation (Myhrer *et al*., 2003; Robbins *et al*., 1998; Meneses *et al*., 1999). Dysfunctional memory occurred after acute lowering in plasma tryptophan (precursor of 5-HT) levels (Riedel *et al*., 2002). The cognitive impairments after TRP depletion were found in healthy volunteers (Riedel *et al*., 2002; Park *et al*., 1994; Rubinsztein *et al*., 2001), as well as in patients with neurological disorders such as Alzheimer disease (Porter *et al*., 2003), bipolar disorders (Sobczak *et al*., 2002) or schizophrenia (Golightly *et al*., 2001). Although modern medicine is well developed in most of the world, large sections of the population in developing countries still rely on the traditional practitioners, medicinal plants and herbal medicines for their primary care. Moreover during the past decades, public interest in natural therapies has increased greatly in industrialized countries, with expanding use of medicinal plants and herbal medicines. Many herbal plants and plant products have shown siginificant cognitive enhancing activity. The herbs that promote the memory and learning are called Medhya herbs. Few of them

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are: *Ginkgo biloba* (Birks *et al*., 2002), *Huperzine A* (Qing-Qi and Sun, 1999), *Bacopamonnieri* (Brahmi) (http://www.celastrusshop.com/memory-enhancers. htm 2008), *Centella asiatica* (Gotu Kola) (Sekar 1996), *Withania somnifera* (Ashwagandha) (Bhattacharya *et al*., 2001) *etc. Mucuna pruriens* is a plant of the Fabaceae family; it is found in tropical regions and used for various purposes in traditional medicine. *Mucuna pruriens* is the popular drug in the Ayurvedic and Unani system of medicine. The plant is famous for the extreme itchiness on contact, particularly with the young foliage and the seed pods due to the presence of 5-hydroxytryptamine (5-HT) ('O'Donnell *et al*., 2011; Sadock *et al*., 2009). The beans of the *M. pruriens* are known to produce the unusual non protein amino acid L-DOPA, a potent neurotransmitter (Roger *et al*., 1998). Common Names of *M. pruriens* are Cowhage, Velvet Bean, Cow-itch, Buffalo bean, velvet bean, mucuna, nescafe, cowage, itchy bean and etc. *Mucuna pruriens* has a long history of use in Ayurvedic medicine. All parts of *Mucuna pruriens* possess valuable medicinal properties and it has been investigated in various contexts, including for its anti-diabetic, aphrodisiac, anti-neoplastic, anti-epileptic, and anti-microbial activities. Number of studies have shown beneficial effects of *Mucuna pruriens* as aphrodiastic, anti-parkinsonism, hypoglycemic, antioxidant, antibacterial, antifungal, and anticancer agents (Chantal Moret 2005; Christmas *et al*., 2011; Muller *et al*., 1998; Pineda *et al*., 2012; Kaizaki *et al*., 2013). Studies pertaining to cognitive enhancer action of *Mucuna prurience* are lacking so far. Therefore present study was planned with the objectives to evaluate cognitive enhancer activity of *Mucuna pruriens* using Y maze model in mice.

MATERIAL AND METHODS

Selection of Animals

The study was conducted in the Department of Pharmacology, King George's Medical University (KGMU), Lucknow. Prior permission was sought from the Institutional Animal Ethics Committee (IAEC) for conducting the study (Project no. 47/IAEC/2013). Adult healthy male Swiss Albino mice of similar physical constitution (in terms of age, body weight), weighing 20-30 g had been used in study. Animals had been obtained from animal house of Indian Institute of Toxicology Research, Lucknow, which is certified by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) for breeding and housing of animals. The animals were housed in Institutional Animal facility under temperature, humidity and light and dark cycle-controlled environment (25±2°C, 70%, 12hrs. Cycle) and were given standard pellet diet and water *ad-libitum.* The maintenance of the animals and the experimental procedures were in accordance with the 'Guide for the Care and Use of Laboratory Animals' (Latest revision in 2011) and the guiding principles of IAEC which strictly adhered to the guidelines of CPCSEA.

Drugs, Dosage and Treatment Groups

Mucuna pruriens (MP) seed extract was procured from Himalaya drug company, Bangalore, India. The standard drug piracetam (UCB India Pvt. Ltd.) was purchased from government authorized medical store. MP and piracetam dissolved in normal saline. Both the drugs were administered per-orally (p.o.). Total 30 mice were divided randomly into control and experimental groups (n=6). Group 1 received the Normal saline and served as the control group, group 2 received the standard drug piracetam (30mg/kg, i.p.) (36), group 3, 4 and 5 received the test drug (MP) in doses of 100, 200 and 400 mg/kg, per-orally.

Y-maze model for learning and memory

Spontaneous Alteration Behaviour (SAB) was assessed using the Y-maze (Saivasanthi *et al*., 2011)**.** The Y-maze is a simple and commonly used behavioral test for spatial working memory and is based on the mouse's natural exploratory instincts. It is used to measure short term memory therefore; spontaneous alteration performance was assessed using Y-maze. Spatial working memory in mice is measured by scoring the number of arm alternations that the mouse makes when it travels to all three different arms of the maze without entering the same arm twice in a row. An arm entry is defined as the body of a mouse except for its tail completely entering into an arm compartment. The sequences of arm entries were manually recorded. An alternation is defined as an entry into all three arms on consecutive choices. The maximum number of spontaneous alternations was then registered as the total number of arms entered minus 2, and the percent alternation calculated as (actual alternations / maximum alternations) x 100 (Drew *et al*., 1973; Conrad *et al*., 1996; Hiramatsu *et al*., 1999; Heo *et al*., 2003). During the entire experiment room level lighting was kept consistent. The procedure was conducted in a sound attenuated room. Every time before placing each animal, the apparatus was thoroughly cleaned.

Stastistical Analysis

All result are expressed as mean ± SD. Data was analyzed using one way analysis of variance (ANOVA), to assess the comparability of the groups assigned to the treatment groups followed by Tukey's multiple comparison tests. P values <0.05 were considered significant.

Table 1. Comparison of % alteration rate and no. of entries in different arms of Y maze

Groups	% Alteration rate (Mean±SD)		No. of arm entries (Mean±SD)	
	DAY 7	DAY 14	DAY 7	DAY 14
NS	62.56±2.78	64.91±5.06	18.50±1.87	15.67±1.86
Piracetam (30 mg/kg)	71.44±5.48*	80.14±6.87**	15.00±1.41*	9.83±1.17**
Mucuna pruriens (100 mg/kg)	63.45±3.74	65.20±5.98	18.17±1.47	16.33±2.16
Mucuna pruriens (200 mg/kg)	67.15±8.60	73.01±7.85	16.33±2.07	13.50±3.51
Mucuna pruriens (400 mg/kg)	73.79±3.13**	79.89±7.01**	14.00±2.10**	9.50±1.05**
p value(ANOVA)	<.01##	< .01##	< .01##	< .01##

(p< .05) ## (p< .01) (ANOVA), * (p< .05), ** (p< .01), (Tukey's multiple comparison test).

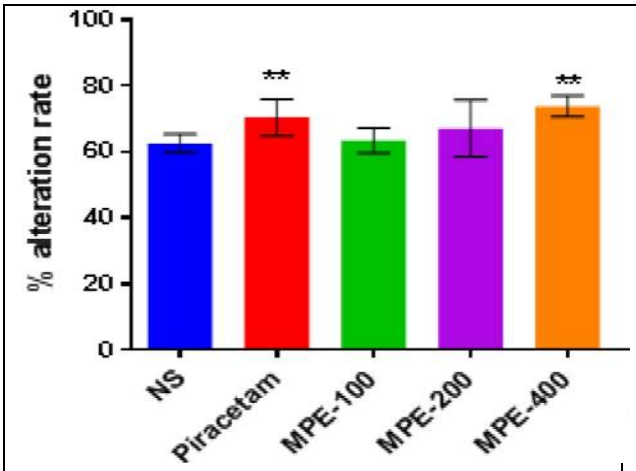

Fig. 1: Effect of *Mucuna pruriens* & Piracetam (30 mg/kg) in Y-maze on day 7.

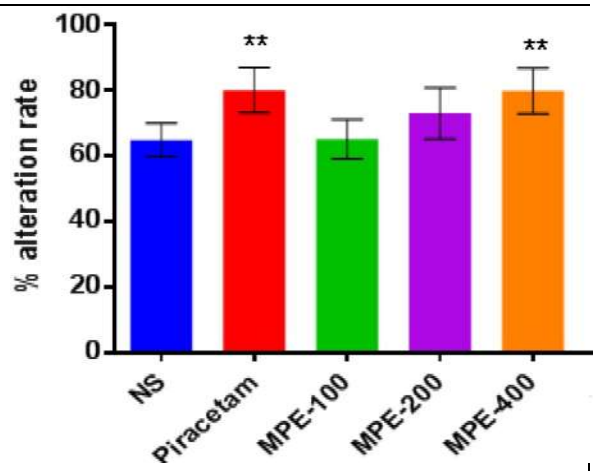

Fig. 2: Effect of *Mucuna pruriens* & Piracetam (30 mg/kg) in Y-maze on day 14.

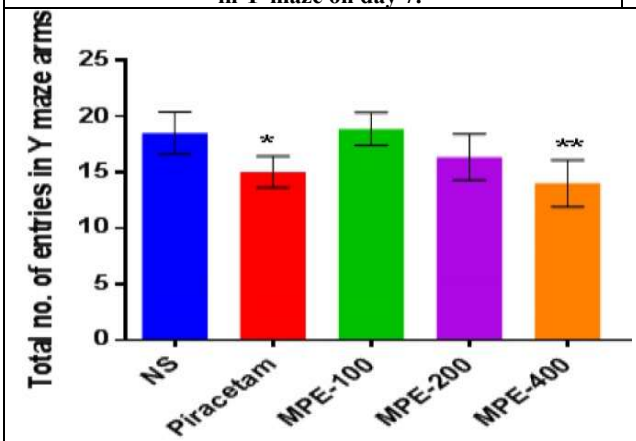

Fig. 3: Effect of *Mucuna pruriens* & Piracetam (30 mg/kg) in Y-maze on day 7.

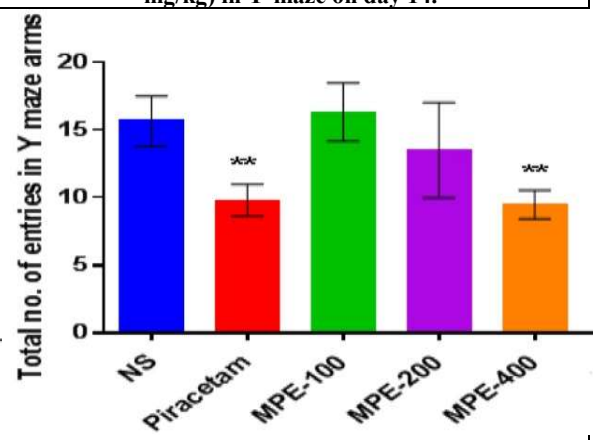

Fig. 4: Effect of *Mucuna pruriens* & Piracetam (30 mg/kg) in Y-maze on day 14.

(p< .05), ** (p< .01), (Tukey's multiple comparison test), compared with control group.
(The column represents the SAB in a 6 min observation period).

RESULT

There is increase in SAB in all the test drugs groups. Highest increase is seen in standard group (Piracetam) and is comparable to increase in MPE in a dose of 400mg /kgbw. MPE at the dose of 400 mg/kg showed significant ($p<0.05$) increase in the SAB (figure 1 & 3) and it showed significant ($p<0.05$) decrease in total number of entries in different arms of Y maze (figure 2 & 4) as compared to control group on day 7 and 14. There is decrease in number of entries from day 7 to day 14 in all the test drugs groups. Highest decrease is seen with MPE in a dose of 400mg/kgbw which is almost similar to decrease in standard group (Piracetam). This decrease is significant in all the test groups as compared to control group ($p <0.05$).

DISCUSSION

Since ages, drugs and natural remedies have been prescribed to enhance memories and learning ability in people. The Indian System of Medicine Ayurveda has a treasury of such memory enhancing drugs. Present time numbers of studies have shown beneficial effects of *Mucuna pruriens*. However, studies pertaining to cognitive enhancer action of *Mucuna prurience* are lacking so far. Toxicity study to determine the safe oral dose of *Mucuna pruriens* was not done in our study because acute toxicity tests, as per OECD 423 guidelines (2010) have already been conducted in many previous studies, reported that extract of *Mucuna pruriens* did not produce any toxicity, or significant behavioural change, or mortality upto an oral dose of 2000mg/kg in albino mice (Lochner *et al*., 2006). In the present study we have evaluated the cognitive enhancer activity of MP in Y-maze. SAB and number of entries in different arms of Y-maze have been used to assess the learning and memory enhancer activity. Increase in SAB and decrease in number of entries in different arms of Y-maze is considered to have a good predictive value in the evaluation of potential learning and memory enhancer agents. In the present study MPE has shown significant increase in SAB on day 7 & 14. Highest increase is seen at a dose of 400 mg/kgbw which is comparable to standard drug (Piracetam). There is a significant decrease in number of entries from day 7 to day 14 in groups receiving MPE in a dose wise manner. Highest decrease is seen with MPE in a dose of 400mg/kgbw which is almost similar to decrease in standard group (Piracetam). Dopamine (DA) has been implicated in learning and memory and its receptors are involved in the control of movement, cognition, emotion, and neuroendocrine secretion (Grabowski 2001). It has been shown that DA has a beneficial impact on spatial working memory (Bubser 1990). The serotonergic system appears to play a role in behaviors that involve a high cognitive demand and in memory improvement or recovery from impaired cognitive performance. These serotonin receptor subtypes are localized on 'cognitive' pathways, the hippocampus and frontal cortex.

The 5HT1A receptor has a high concentration in the limbic system, where autoreceptors influence cognitive functions. Stimulation of 5-HT1A receptors has detrimental effects on learning and working memory, whereas their inactivation selectively antagonizes these effects. Different cerebral structures that are rich in 5-HT receptors (such as the lateral septum, the hippocampus, the frontal cortex) are involved in the interaction between cognition and emotion, which includes mnemonic as well as attentional components (Buhot 1997)**.**

Conclusion

Mucuna pruriens increased SAB and decreases Number of entries in the mouse Y-maze model. Our study suggests that *Mucuna pruriens* possess potent learning and memory enhancing properties.

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