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Effects of *Mangifera indica* fruit extract on cognitive deficits in mice

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Abstract: *Mangos are a source of bioactive compounds with potential health-promoting activity. The present work was undertaken to evaluate the ethanolic extract of Mangifera indica L. fruit on cognitive performances. The models used to study the effect on cognitive performances are step down passive avoidance task and elevated plus maze task in mice. Chronic treatment (7 days) of extract and vitamin C significantly ($p < 0.05$) reversed the aging and scopolamine induced memory deficits in both paradigms. Preliminary phytochemical screening revealed the presence of free sugars, saponins, tannins, and flavonoids. The results suggest the extract contained pharmacologically active principles that are memory-enhancing in nature.*

Key words: *Mangifera indica, Cognitive deficits, Vitamin C, Scopolamine, Antioxidants*
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Introduction

Dementia is one of the age related mental problem and characteristic symptom of various neurodegenerative diseases including Alzheimer's disease. The disorder, which affects men and women equally, is characterized by progressive deterioration of cognitive functions, such as memory, language and visuospatial orientation. Associated symptoms are mood and behavioral changes with advancing age (Foster *et al*., 1994). Natural aging is known to deteriorate memory in human beings (Petersen, 2004). However, the nature of the casual factors responsible for deleterious changes is poorly understood. Oxygen free radicals, the harmful byproducts of oxidative metabolism are known to cause organic damage to the brain because the brain is believed to be particularly vulnerable to oxidative stress due to a relatively high rate of oxygen free radical generation without commensurate levels of antioxidative defenses (Brewer, 1998; Sohal *et al*., 1990), which may be responsible for the development of dementia or Alzheimer's disease in elderly (Nagy, 2001; Smith and Luo, 2003). Natural products represent a reservoir of diverse templates; and increasingly, medicinal plants are being used in the treatment of various neurodegenerative disorders (Stocker, 1994; Hollman *et al*., 1996). Several reports suggest that certain phenolic antioxidants attenuate neuronal cell death induced by oxidative stress (Schroeter *et al*., 2000; Youdin and Joseph, 2001; Perez-Perez and Rodriguez-Malaver, 2005; Mancuso *et al*., 2007).

It is revealed that *Mangifera indica* L. (family Anacardiaceae) extract (Vimang) protects from the oxidative damage induced by oxygen-based free radicals as shown in several in vitro test systems conducted (Sanchez *et al*., 2003; Pardo-Andreu *et al*., 2005; Amazzal *et al*., 2007; Hernandez *et al*., 2007).

Investigation of the potential effects of fruit and vegetable components on cognitive functions have until recently, been limited. With this in mind, we studied the effects of *Mangifera indica* fruit extract on cognitive performances in aging mice and scopolamine induced cognitive deficits in young mice.

Materials and Methods

Plant material and extraction: Ripe fruit of *Mangifera indica* L. were purchased locally. The ripe fruit was extracted successively with petroleum ether, chloroform, ethanol followed by water. The ethanolic crude extract was filtered and concentrated by rotavapour. The yield of the extract was 22% w/w. The extract was then stored in a desiccator.

Animals: Swiss albino mice (*Mus musculus albinus*) of either sex of 3 months (young) and 14 months old (aged), weighing 20-25 g and 38-42 g, respectively, were obtained from Central Animal House, Jamia Hamdard, New Delhi, India. They were housed in an environmentally regulated room on a 12 hr light: 12 hr dark cycle with 25 ± 2°C and had free access to food and water. The experimental protocol was approved by the Institutional Animal Ethical Committee and experiments conducted according to the CPCSEA, India guidelines on the use and care of experimental animals. Experiments were carried out between 09:00 and 18:00 hr.

Experimental design: To evaluate the effect of chronic treatment of ethanolic extract of ripe fruit of *Mangifera indica*, aged mice were randomly distributed into four groups. The first group of animals received only specify treatment perorally for a period of 7 days. Subsequent two groups of animal received varying doses of mango ripe fruit extract (250 and 500 mg kg^{-1} perorally once a day) for a period of 7 days. The extract was suspended in 5% tween 80. The last group received vitamin C (250 mg kg^{-1}, perorally) as a standard drug. Similarly treatment was also performed in different groups of young mice. In young animals, amnesia was induced by

administration of scopolamine (1 mg kg^{-1}, *i.p.*) on 7th day and the step down latency (SDL) and Transfer latency (TL) recorded. Retention was recorded after 24 hr. On 7th day, after 60 min of administration of doses, scopolamine was administered and SDL and TL noted after 30 minute. On the next day (day 8), animals tested for their retention using passive avoidance and elevated plus maze task.

Elevated plus maze test: Acquisition and retention of memory was evaluated by using the elevated plus maze learning task, which measures spatial long-term memory (Reddy and Kulkarni, 1998). Transfer latency (TL) (the time in which the animal moves from the open arm to the enclosed arm) was utilized as an index of learning and memory processes. The procedure was basically identical to that described by Itoh *et al.* (1991). The elevated plus maze consisted of two open arms (16 X 5 cm) and two enclosed arms (16 X 5 X 12 cm) with an open roof. The maze was elevated to a height of 25 cm from the floor. The animals were placed individually at the end of either of the open arms and the transfer latency was noted on the first day. To become acquainted with the maze, the animals were allowed to explore the plus maze for 20 seconds after reaching the closed arm. On the second day, 24 hr after the first exposure, transfer latency was again noted. A long latency period to reach enclosed arm indicates poor retention compared to significantly shorter latencies.

Passive avoidance test: A step-down type passive avoidance test apparatus was used to evaluate the effects of extract on learning and memory as described by Reddy and Kulkarni (1998) and Raghavendra *et al.* (1999). The apparatus consisted of an electric grid with a centrally located shock free platform (10 X 7 X 30 cm). During the training session, each mouse was gently placed on platform, as the mouse turned down the platform foot shock (2 mA) was delivered for 2 seconds. The mouse was removed from the enclosure immediately after receiving the shock to their respective home cages. The step down latency (SDL) was recorded from the time the mouse was placed on platform until it stepped down to the platform. The retention test was carried 24 hr after training, in the similar manner, except that the electric shocks were not applied to grid floor. Short latencies indicate poor retention compared to significantly longer latencies.

Locomotor activity test: The animal locomotor behavior was monitored using actophotometer, described by Reddy and Kulkarni (1998). Before subjecting the animals to cognitive tasks, they were individually placed in actophotometer and the ambulatory activity registered for five-minute period. The locomotor activity was expressed in terms of total photobeam count 5 min per animal.

Statistical analysis: Results are expressed as means ± SE The data were analyzed using one-way ANOVA followed by Dunnet's test. The criterion for statistical significance was $p<0.05$.

Results and Discussion

The results of the study are presented in Fig. 1 and 2. The oral treatment with the alcoholic extract of *Mangifera indica* (MI) ripe fruit at doses from 250 to 500 mg kg^{-1} significantly ($p<0.05$) decreased the transfer latency (TL) in aged and scopolamine treated young mice compared with respective controls (Fig. 1), indicating the memory retention effect of extract. In passive avoidance task, the MI ripe fruit extract significantly ($p<0.05$) increased the step down latency (SDL) reflecting the memory retention effect of alcoholic extract (Fig. 2). In order to check the possible interference of general sensorimotor function, motor behavior during cognitive tasks, mice were tested with an actophotometer. In the present study, MI (250 and 500 mg kg^{-1}, perorally) and vitamin C (250 mg kg^{-1}, perorally) did not show any significant change in locomotor function of animals (Scores 182.47 ± 10.27 s and 175.89 ± 9.67 s) and (168.54 ± 9.45 s) respectively as compared to control group (Scores 186.55 ± 11.75 s) when tested using an actophotometer.

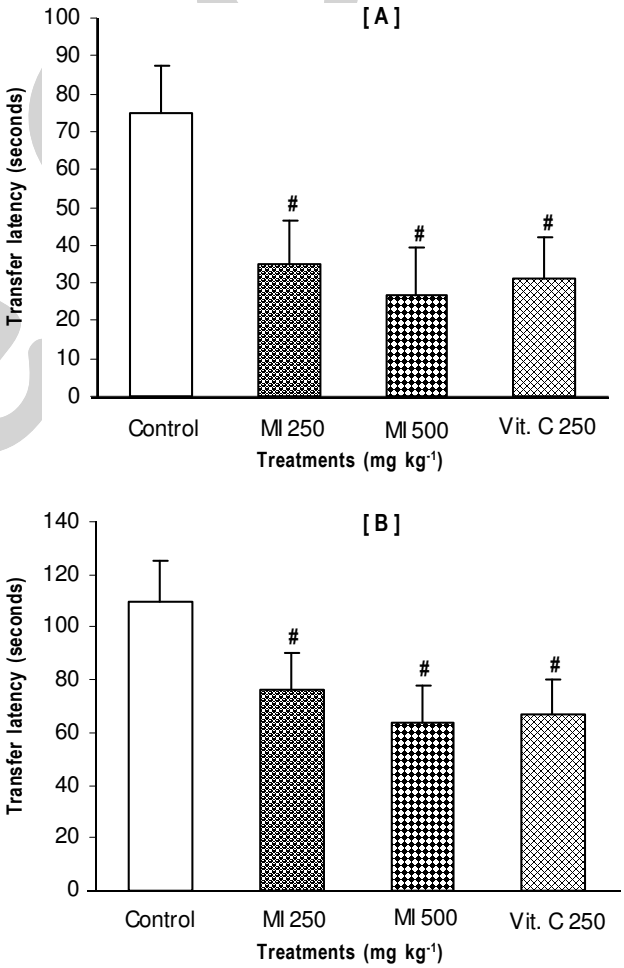

Fig. 1: Effect of chronic administration of *Mangifera indica* (MI) extract (250 and 500 mg kg^{-1}) and vitamin C (vit. C 250 mg kg^{-1}) on Transfer latency (TL) in aged mice (A) and in young mice (B). Values are expressed as mean ± SE. $^{\#}p<0.05$ vs control mice, n = 10 animals

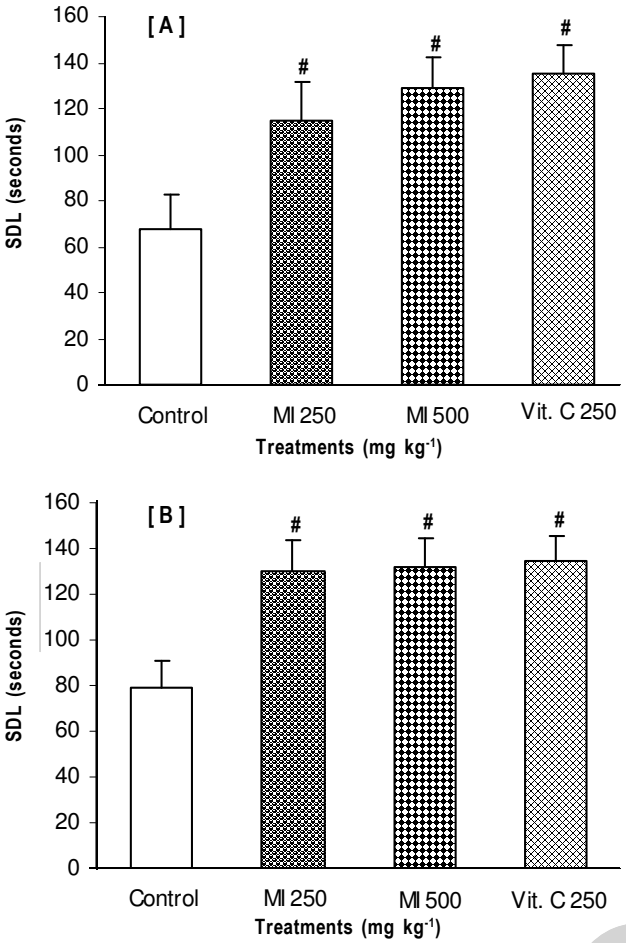

Fig. 2: Effect of chronic administration of *Mangifera indica* (MI) extract (250 and 500 mg kg^{-1}) and vitamin C (vit. C 250 mg kg^{-1}) on Step down latency (SDL) in aged mice (A) and in young mice (B). Values are expressed as mean ± SE $^{\#}p < 0.05$ vs control mice, n = 10 animals

Cognitive dysfunction such as learning impairment and delayed amnesia are the most striking age-related changes observed in human being and animals (Foster *et al*., 1994; Gray *et al*., 2008). These types of deficits probably are due to the vulnerability of the brain cells to increased oxidative stress during aging process (Floyd, 1999; Nagy, 2001). Recently it is reported that antioxidants are effective in the amelioration of dementia process, suggesting the involvement of oxidative stress component in dementia or AD (Youdin and Joseph, 2001; Perez-Perez and Rodriguez-Malaver, 2005; Mancuso *et al*., 2007).

The results of this study clearly indicate that oral administration (7 days) of MI ripe fruit extract and vitamin C to aged mice and young mice reverse impairment of memory retention in one trial step down avoidance and elevated plus maze task. Mangos are a source of bioactive compounds with potential health-promoting activity. Data from literature also support that MI has potent antioxidant profile (Sanchez *et al*., 2003; Pardo-Andreu *et al*., 2005). It is revealed from several studies that MI extract consists of a defined mixture of components (polyphenols, terpenoids, steroids, fatty acids and microelements) and a xanthone (mangiferin) as a main component (Rodeiro *et al*., 2006; Wilkinson *et al*., 2008). This extract has antioxidant action proved in experimental models in both in vitro and *in vivo* assays (Prabhu *et al*., 2006; Amazzal *et al*., 2007; Hernandez *et al*., 2007).

Considering the fact that the dementia associated with increased brain oxidative stress during brain aging and its reversal by antioxidants (Clausen *et al*., 1989; Carney *et al*., 1991; Socci *et al*., 1995; Gray *et al*., 2008). Our results suggest that the antiamnesic effect of MI ripe fruit extract in present study could be due to its antioxidant action. Subsequent studies are, therefore, necessary in order to verify the *Mangifera indica* mechanism of action, to elucidate the active principles involved with its antiamnesic effect.

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