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NATURAL FLAVONOID ATTENUATES MANGANESE-INDUCED MANGANISM IN RATS

Harihara Behera* and Abhisek Pal

School of Pharmaceutical Sciences, Siksha 'O' Anusandhan University Deemed To Be, Bhubaneswar-, 751003, Orissa, India.

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***Corresponding Author**
Harihara Behera
School of Pharmaceutical Sciences, Siksha 'O' Anusandhan University Deemed To Be, Bhubaneswar-, 751003, Orissa, India.

ABSTRACT

Manganese (Mn) is a metal required by biological systems. However, environmental or occupational exposure to high levels of Mn can produce a neurological disorder called manganism. The neuroprotective actions of dietary flavonoids involve a number of effects within the brain, including a potential to protect neurons against injury induced by neurotoxins. The present study was designed to investigate the effects of long term low-dose exposure to Mn in drinking water on behavioral and biochemical parameters in rats and to determine the effectiveness of flavonoid in attenuating the effects of Mn. After 30 days of continuous treatment with $MnCl_2$ (10 mg/kg), rats exhibited clear signs of neurobehavioral toxicity depicted in terms of catalepsy score using standard bar tes, activity score using actophotometer, manganese tissue analysis, neurohistopathology, neuroimaging and biochemical analysis. Our findings show that oral exposure to Mn may cause neurobehavioral abnormalities in adult rats that could be efficiently alleviated by concomitant supplementation of flavonoid in animal feed.

KEYWORDS:

INTRODUCION

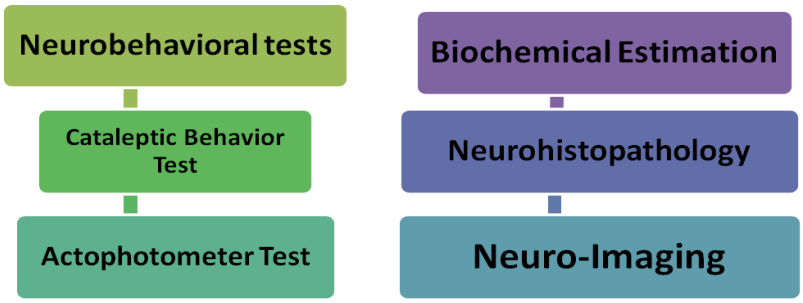
Manganese (Mn) is the twelfth most abundant element in the earth's crust and is naturally present in the environment and food. Mn finds its huge industrial application in electronic components, chemical and battery industries, iron and steel production, manufacture of dry cell batteries, oxidant in the production of hydroquinone, manufacture of glass, textile bleaching, oxidizing agent for electrode coating in welding rods, matches and fireworks; and

tanning of leather. Exposure to elevated manganese occurs during mining, welding, smelting, dietary overexposure and other industrial anthropogenic sources. Exposure to manganese compounds results in neurotoxicity and neurodegenerative diseases. Miners and welders leading to neurological dysfunction associated with dystonic movement's cortical structures and accumulation in basal ganglia leading to idiopathic Parkinson's disease has previously been established.

The present study was designed to investigate the effects of long term low-dose exposure to Mn in drinking water on behavioral and biochemical parameters in rats and to determine the effectiveness of flavonoid in attenuating the effects of Mn in neurotoxicity and neurodegeneration.

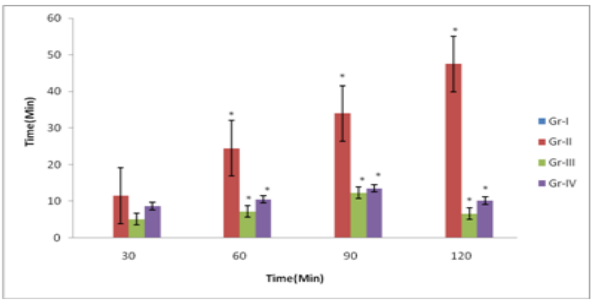
METHODS

Groups	Treatment Solution
I(Control)	Sterile saline
II	$MgCl_2$ 10 mg/kg (p.o)
III	$MgCl_2$10 mg/kg+ Naringin 25 mg/kg (p.o)
IV	$MgCl_2$10 mg/kg+ Vitamin E 25 mg/kg (p.o)



RESULTS

Fig I: Effect of the test drug Naringin (25 mg/kg, p.o.) on cataleptic score in $MgCl_2$ 10 mg/kg (p.o), i.p induced rats



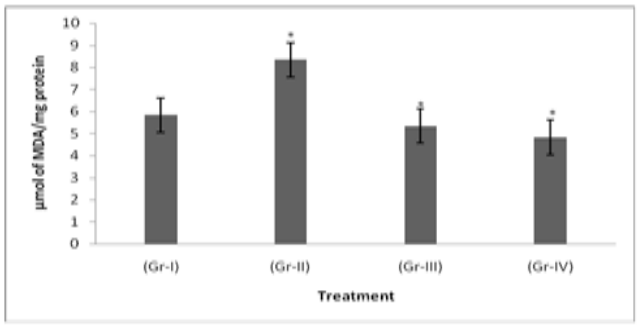
mean ±SEM. Statistical significant test for comparison was done by one way ANOVA followed by Dunnet's t-test. *p<0.05

Table I. Effect of the test drug Naringin (25 mg/kg, p.o.) on activity score in $MgCl_2$ 10 mg/kg (p.o), induced rats using Actophotometer test

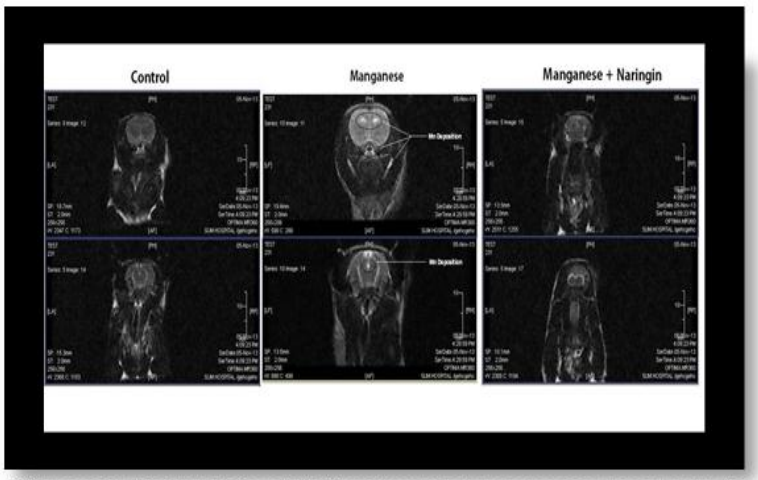
Groups	Treatments	Activity Score (Mean±SEM)
I	Sterile saline	249.16±3.40
II	$MgCl_2$ 10 mg/kg (p.o)	61.83 ±1.86*
III	$MgCl_2$ 10 mg/kg+ Naringine 25 mg/kg (p.o)	238.33±1.86*
IV	$MgCl_2$ 10 mg/kg+ Vitamin E 25 mg/kg (p.o)	224.16±1.83*

mean ±SEM, *p<0.05

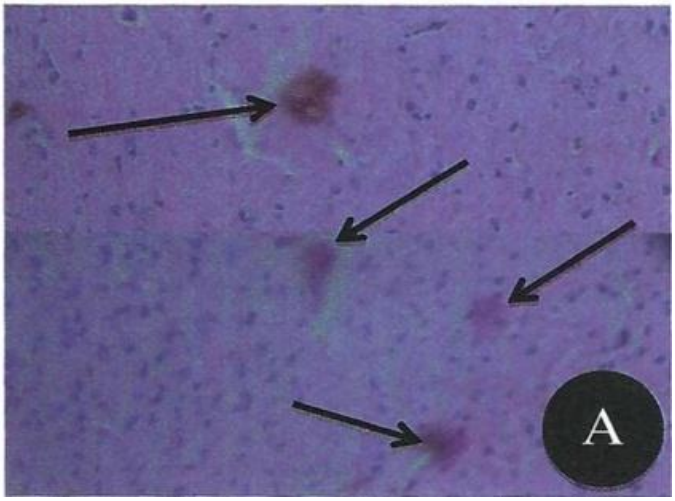
Fig II: Effect of the test drug Naringin (25 mg/kg, p.o.) on lipidperoxidation level in $MgCl_2$ 10 mg/kg (p.o) induced rats



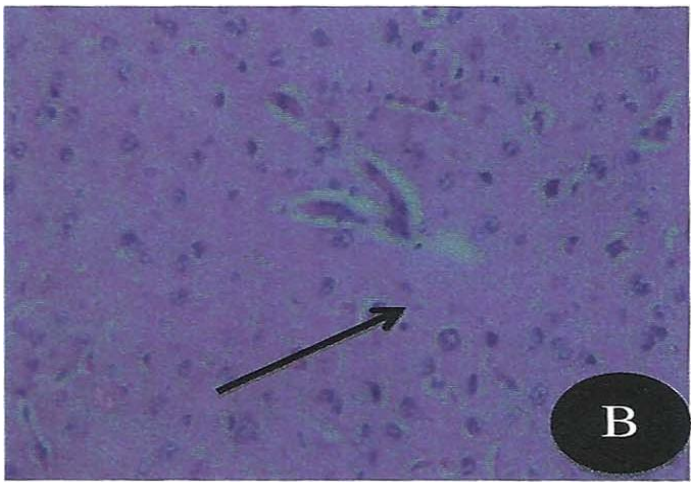
mean ±SEM, *p<0.05



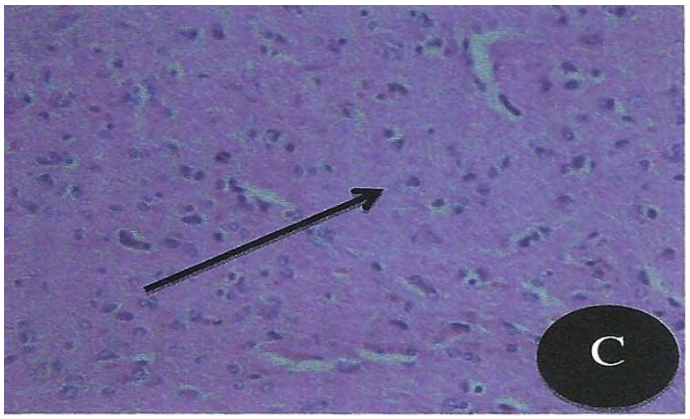
MRI images in this study indicate high Mn concentrations in manganese treated rat in the hippocampal cortex, as well as in other crucial subcortical structures – the brain stem and midbrain, which is decline in manganese +Naringin treated rat.



A. Striatal section of $MgCl_2$ 10 mg/kg (p.o) treated rat.



B. Striatal section of $MgCl_2$ 10 mg/kg (p.o) + Naringin 25 mg/kg(p.o) treated rat.



C. Striatal section of $MgCl_2$ 10 mg/kg (p.o) + Vitamin-E 25 mg/kg (p.o) treated rat.

CONCLUSION

Oxidative stress plays a major role in Mn-induced neurotoxicity and two possible putative mechanisms may lead to oxidative stress, as an outcome of ROS accumulation: interference with normal mitochondrial respiration and/or oxidation of DA and other catecholamines. Given the recognition that oxidative stress plays a key role in Mn toxicity, several biomarkers of oxidative stress, GSH were determined. Naringin effectively reversed the Mn-induced reduction in brain GSH depletion. Our study suggests that Naringine and vitamin E can alleviate manganism symptoms and offers a new approach to its treatment and prevention.

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