EFFECTS OF *MORINDA CITRIFOLIA* LINN (NONI) AND TAHITIAN NONI® JUICE (TNJ) ON LOCOMOTOR ACTIVITY IN MICE

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ABSTRACT

Noni fruit extract and juice (*Morinda citrifolia L*., Family: Rubiaceae) had long been known as a medicinal plant in folklore medicine in tropical countries and Pacific islands. To date, the available scientific knowledge was focused on different pharmacological effects. It was claimed to have beneficial effect on drug addiction by Noni fruit extract and its juice in animal studies. Keeping this in mind we investigated whether the noni fruit extract and noni beverages contained any effect on locomotion in mice using Actimeter (a standard test for locomotor activity). We found that the administration of single dose of *Morinda citrifolia* extract (MMC) at varying doses (0.5, 1, 3 and 5 g/kg p.o.) 60 min before the testing and Tahitian noni juice (TNJ) 100% made available as a source of drinking water for a period of 24 hours before the test day produced no significant effect on animal's locomotion and behavior when compared with control group. The extract did not exhibit any toxic effects. There was no mortality and change in animal behavior seen. The current results suggest that MMC and TNJ are safe and can be utilized for further neuropharmacological research.

Key words: *Morinda citrifolia*, TNJ, locomotor activity, behavioral effects, Actimeter.

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INTRODUCTION

Locomotion, that is active propulsive movement of the body in space, is a vital motor function. Recent studies of mechanisms underlying control of locomotion in different directions have greatly expanded our knowledge about locomotor system and can contribute to improvement of locomotion and balance control in patients (Kiehn O., 2013).

Morinda citrifolia Linn. (Noni) has been utilized as diet source, medicine, and fabric dyes by Polynesian people (Pandy et al, 2016, Dixon et al., 1999). Traditionally, *M. citrifolia* has been widely used as prophylaxis and treatment of many CNS disorders such as anxiety, depression, and psychosis and drug dependence. In earlier study by our research group, MMC was

reported for anxiolytic and antidepressant-like activity (Narasingam et al., 2017) anti-psychotic-like activity (Pandy et al, 2012) and anticraving effect in opposition to heroin, ethanol and methamphetamine dependence using conditioned place preference test in rats and mice (Pandy et al, 2012, Narasingam et al., 2017; Khan et al, 2016) and it also showed anticancer activity (Gopal et al, 2022).

In addition, Noni has also recently been reported to protect against scopolamine-induced and β-amyloid (25–35)-induced memory impairment in animals (Muralidharan et al., 2010, Pachauri et al., 2012). Pretreatment with different doses of Noni fruit extract in STZ-injected mice improved spatial memory and conditioned avoidance memory, as evidenced by

improved performance in both tests (Pachauri et al, 2013). In addition, no significant difference in spontaneous locomotor activity was observed among different groups. This observation excludes the possibility that an alteration in locomotor activity may have contributed toward the observed behavioral changes in mice following STZ/Noni administration (Pachuri et al, 2013). Studies have shown that Noni contains polyphenolic compounds such as quercetin, rutin, scopoletin, and kaempferol, which are reported to have potent antioxidant and neuroprotective effects in animal models (Pandy et al, 2014). In neuropharmacological research, the result of drug candidates on locomotion is important to rule out the possibility of interaction on locomotion that affects the results (Pachauri et al, 2013). Therefore, in this study, we evaluated the effect of MMC and TNJ on locomotor activity in mice by employing Actimeter.

MATERIALS AND METHODS

Animals

Male ICR mice (UKM, Kuala Lumpur, Malaysia) weighing 25 to 30 g were housed in polycarbonate cages in a group of four per cage for at least 7 days before use and were maintained on a 12:00/12:00- h light/dark cycle (lights off at 7:00 pm), a temperature of 20 to 22 ^{0}C, and a humidity of 45 to 60%. They were provided with free access to food pellets and tap water. The mice were acclimatised to the housing conditioned and handled for 7 days before the start of the

experimental session, and an effort was made to minimise animal suffering. All experimental procedures were approved by the Animal Care and Use Committee, Faculty of Medicine (FOM IACUC) University of Malaya, Kuala Lumpur approved the experimental protocol (Ethics No. 2013-12-03/PHAR/R/VP) and care of the animals was taken as per guidelines of the Council for International Organization of Medical Sciences (CIOMS) on animal experimentation.

Drugs

All the drug solutions were prepared fresh in normal saline and administered per oral

(p.o.) in a constant volume of 1 ml/100 g body weight of the animal. The MMC was suspended in 1% w/v sodium carboxymethyl cellulose (CMC) solution and administered orally (p.o) at doses of 0.5, 1, 3, and 5 g/kg. Commercial noni fruit juice, Tahitian Noni® juice (TNJ) was obtained from Morinda International Inc, Malaysia.

TNJ is a fruit mixture of 89% noni fruit puree and 11% of grape and blueberry juice concentrate and natural flavours because 100% pure noni juice is unpalatable.

Acetimeter test

In order to facilitate adaptation, mice were held for 2 weeks in the laboratory facilities between the delivery from the supplier and testing in the behavioural trials. Spontaneous locomotor activity of mice was measured by means of an actimeter (INFRA-RED ACTIMETER SYSTEM ACT_01, Orchid scientific, India) composed of one square frame, frame stand & hole board plate. The frame is equipped with 32 IR cells (ACT_01). In model ACT-01, 16 cells are

on X-axis & 16 cells are on Y-axis. The Infra-red cell work at wave length of 950 mm & its information is multiplexed at a rate of 40 Hz. On the day of the test, mice were transported to the test enclosure and allowed to adapt to the actimeter apparatus for 30 min prior to the treatment. Each mouse was tested in the actimeter only once, and naive mice were used for experiment. All tests were conducted under dim red light, under light/dark cycle. The total number of ray's interruption was recorded over a period of 10 min. The actimeter test was performed to examine the effect of drugs on spontaneous locomotor activity of mice.

RESULTS

Effect of MMC and TNJ (100%) on locomotor activity

As shown in figures 1 data showed that single-dose administration of MMC (0.5, 1, 3 and 5 g/kg p.o.) 60 min before the testing and TNJ 100% made available in drinking water produced no significant effect on number of rays interruption [$F(5, 24) = 1.964$, $p > 0.05$; n.s] as seen with baseline values [$F(5, 24) = 1.515$, $p > 0.05$)].

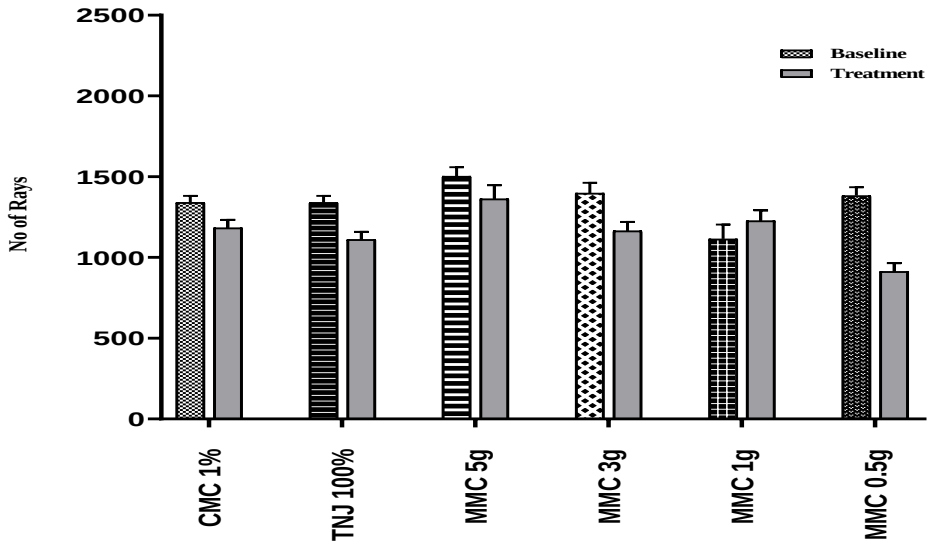

Figure.1: (Mean ±S.E.M.) Baseline values for locomotor activity of all six groups of mice treated with vehicle (VEH) verses effects of acute p.o. administration of MMC (0.5, 1, 3 and 5g,) 60 min before the test and TNJ 100% in drinking water on spontaneous locomotion in the actimeter test. Total activity counts for 10 min. These results are cited as mean ± SEM (n = 5). Statistical analysis was performed by a one-way ANOVA followed by a Dunnett's test.

DISCUSSION

The various neuropharmacological activities such as antidepressant, anxiolytic, antipsychotic, anticraving against ethanol, heroin and methamphetamine and analgesic activities of noni fruit extract and its juice have been reported in the literature. The

present results showed that a varying doses of Noni fruit extract (MMC) and Noni juice (TNJ) made available in drinking water did not change the locomotion of animals which indicates no motor impairment caused by noni fruit extract and juice.

Recent study showed anticancer activity of Noni fruit (Gopal et al, 2022). Noni fruit roots extract have been reported for sedative and analgesic activities in mice and postulated the involvement of a central opioid receptor mechanism (Khan et al, 2016). Furthermore, noni juice has been reported to have nootropic activity in stress-induced cognitively impaired mice using the Morris water maze (Muto et al, 2010). An acute oral toxicity study of MMC was performed and described in our previous publication where no toxic effects of MMC were observed up to a dose of 20 g/kg (Pandy et al., 2012).

Drugs that affect the motor activity of animals can infuence CPP result. However, Pachauri et al. (2013) demonstrated that there was no significant difference in spontaneous locomotor activity in mice treated with a noni fruit extract (Khan et al., 2016). Similarly, rats treated with noni juice orally for 15 days exhibited no alteration in motor activity (Kalandakanond et al., 2004). The present results are corroborated with Pachauri et al. (2013) in which no significant difference in spontaneous locomotor activity in mice treated with a noni fruit extract was observed (Khan et al., 2016). Similarly, rats treated with noni juice orally for 15 days exhibited no alteration in motor activity (Kalandakanond et al, 2004). We therefore suggest that Noni fruit extract (0.5-5 g/kg, p.o.) and TNJ (100%v/v) in drinking are safe to use in neuropharmacological studies.

The major phytoconstituents of MMC were characterized and quantified as scopoletin (18.95 µg/mg) and rutin (1.66 µg/mg) in a report (Pandy et al., 2014) and claimed that these active phytoconstituents of Noni i.e scopoletin and rutin are responsible for the various pharmacological activities of noni including its antidopaminergic activity (Deng et al., 2007, Pandy et al., 2014). Although the present work could not delineate the active phytoconstituents that are responsible for the its effects we hypothesize that these positive behavioral effects are likely due to the presence of phytoconstituents of MMC. Clearly, further studies using scopoletin and rutin per se on ethanol-induced CPPs in experimental animals are warranted and are currently underway in our laboratory.

CONCLUSION

The present study demonstrates that MMC and TNJ does not produced any side effects on locomotor activity of mice by using Actimeter therefore present finding suggest that MMC and TNJ are safe for use in research and it could motivate more researchers for further work.

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