UNIVERSITI PUTRA MALAYSIA

EFFECTS OF MITRAGYNINE FROM *MITRAGYNA SPECIOSA* Korth. LEAVES ON WORKING MEMORY IN MICE

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MASTER OF SCIENCE
UNIVERSITI PUTRA MALAYSIA

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Master of Science

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Science

EFFECTS OF MITRAGYNINE FROM *MITRAGYNA SPECIOSA* Korth. LEAVES ON WORKING MEMORY IN MICE

By

EVHY APRYANI

MARCH 2011

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Faculty : Medicine and Health of Sciences

Repeated exposure to opiates can lead to deficits in cognitive function. A study in 2000 reported that opioid users have the risk for the brain damage. In the present study, we examined the working memory effects of mitragynine extracted from *Mitragyna speciosa* mature leaves using object location task and the motor activity in open field test. Mitragynine of the dose 5, 10 and 15 mg/kg were administered intraperitoneally (IP) to mice for 28 consecutive days and evaluated on day 28 after the last dose treatment. Scopolamine was used as the positive control drug. After the completion of behavioral study, mice were sacrificed and the brain was used to evaluate any changes in hippocampal morphology and in the expression of N-Methyl-D-aspartic Acid Receptors-1 (NMDAR1) by using immunohistochemical method.

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It was observed, that the administration of mitragynine significantly reduced the locomotor acitivity in open-field test compared with vehicle ($p < 0.05$). Some studies have been reported an association between exploratory behavior to the level of cognitive function. in object location task, mitragynine treated mice did not show any significance discrimination between the object that had changed position than the object that had remain in a constant position ($p > 0.05$). The analysis of the results obtained indicated that mice with cognitive impairment will spend more time exploring the familiar object than the novel one. An absence of any difference in the exploration of the two objects during the second phase can be interpreted as a memory deficit. Histological study did not show any morphological changes but immunohistochemical study showed down-regulation in the expression of NMDAR1. Our results suggested that chronic administration of mitragynine may alter the cognitive behavioral function in mice, while preserving the brain morphology.

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Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

EFFECTS OF MITRAGYNINE FROM *MITRAGYNA SPECIOSA* Korth. LEAVES ON WORKING MEMORY IN MICE

Oleh

EVHY APRYANI

MAC, 2011

Pengerusi : Mohammad Taufik Hidayat Baharuldin, PhD

Fakulti : Perubatan dan Sains Kesihatan

Paparan berulang opiat boleh menyebabkan defisit dalam fungsi kognitif. Sebuah kajian pada tahun 2000 melaporkan bahawa pengguna opioid mempunyai risiko kerosakan otak. Penelitian ini bertujuan untuk mengetahui kesan mitragynine yang diekstrak daripada daun *Mitragyna speciosa* matang terhadap memori kerja mencit. Kesan kognitif dipelajari dengan menggunakan lokasi objek tugas dan aktiviti motor di uji lapangan terbuka. Mitragynine 5, 10 dan 15 mg / kg dan dikendalikan oleh intraperitoneal (IP) selama 28 hari berturut-turut dan diuji pada hari ke-28 selepas rawatan dos terkini. Skopolamin digunakan sebagai kawalan positif dadah. Setelah selesai mengkaji perilaku, mencit dikorbankan dan otak digunakan untuk menilai perubahan histologis dan ekspresi NMDAR1 menggunakan kajian imunohistokimia.

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Dalam kajian ini terdapat pengaruh yang menonjol pada aktiviti lokomotor mencit. Mitragynine secara signifikan mengurangkan aktiviti lokomotor dalam uji lapangan terbuka berbanding dengan control ($p < 0.05$). Di lokasi objek tugas, mitragynine tidak menunjukkan adanya diskriminasi signifikansi antara objek yang berubah kedudukan dari objek yang tetap dalam posisi yang sama ($p > 0.05$). Pengajian histologi tidak menunjukkan perubahan morfologi tetapi kajian imunohistokimia menunjukkan perubahan dalam ekspresi NMDAR1 di hipokampus.Keputusan kajian kami menunjukkan bahawa rawatan kronik mitragynine boleh menukar perilaku fungsi kognitif pada mencit.

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I certify that an Examination Committee has met on date/month/year to conduct the final examination of Evhy Apryani on her Master of Science thesis entitle "The effects of mitragynine from *Mitragyna speciosa* Korth. leaves on working and memory function in mice" in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) Regulations 1981. The Committee recommends that the student be awarded the Master of Science.

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DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

EVHY APRYANI

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