UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

Announcement:

All interested members of the university community are invited to attend the Final Oral Examination for the degree of ***Master of Science*** *of*

SHOSHANA BUCKHALTER

on Thursday, April 22, 2021 at 9:30 a.m. (online)

Thesis Title: **The antidepressant and analgesic effects of kratom are accompanied by changes in low frequency oscillations but not DeltaFosB accumulation**

Examination Committee:

Dr. Annette Nassuth, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Melissa Perreault, Dept. of Biomedical Sciences
Dr. Jibran Khokhar, Dept. of Biomedical Sciences
Dr. Shaun Sanders, Dept. of Molecular and Cellular Biology

Advisory Committee:
Dr. Melissa Perreault (Co-Advisor)
Dr. Tariq Akhtar (Co-Advisor)
Dr. Jibran Khokhar

Abstract: *Mitragyna speciosa* (kratom) is a tree native to Southeast Asia that is believed to have medicinal properties to both improve mood and relieve acute and chronic pain. Kratom contains many alkaloids, yet most studies have focused solely on two alkaloids, mitragynine and its derivative 7-hydroxymitragynine. In this study the dose-dependent effects of a purified alkaloid kratom extract on neuronal oscillatory systems function and behaviour were therefore evaluated. We first generated a purified alkaloid isolate from kratom leaves obtained from a cultivar grown under controlled conditions and characterized the major alkaloids present in the extract using traditional analytical methods. Male rats were administered a low (0.5 mg/kg) or high (1 mg/kg) dose of the kratom extract for 7 days and local field potential recordings taken on the first and final day of injections. Following recordings, behavioural testing in the forced swim test and the tail-flick test were performed to evaluate antidepressant and analgesic drug properties. Kratom-induced changes in ΔFosB expression, a posited marker of addiction, in response to the high dose of kratom were also evaluated. Acute or repeated low dose kratom suppressed ventral tegmental area (VTA) theta oscillatory power whereas acute or repeated high dose kratom increased delta, and reduced theta, power in the nucleus accumbens (NAc), prefrontal cortex (PFC), cingulate cortex (Cg) and VTA. The repeated administration of low dose kratom additionally elevated delta power in PFC, decreased theta power in NAc and PFC, and suppressed beta and low gamma power in Cg. Suppressed high gamma power in NAc and PFC was seen selectively following repeated high dose kratom. Overall, both doses of kratom elevated coherence with the most robust effects in the NAc-PFC, VTA-NAc, and VTA-Cg pathways. Acute or repeated low dose kratom was antidepressant whereas both doses of kratom had analgesic effects. No kratom-induced changes in ΔFosB expression were evident in any region. These results support a role for kratom as having both antidepressant and analgesic properties that are accompanied by specific changes in neuronal circuit function. However, the absence of drug-induced changes in ΔFosB expression suggest either a lack of addictive properties of the extract or that the drug may circumvent this cellular signaling pathway. Further studies will be required to explore more in depth the addictive potential of the whole kratom extract.

Curriculum Vitae: Shoshana completed her Bachelor of Science (Hons.) at the University of Guelph in April 2019. She then started her M.Sc. in the labs of Dr. Perreault and Dr. Akhtar in May of the same year.

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