

The College of Graduate Studies and the College of Medicine and Health Sciences**Cordially Invite You to a****Master Thesis Defense**Entitled

CANAGLIFLOZIN AMELIORATES AUTISTIC-LIKE FEATURES AND MITIGATES BRAIN OXIDATIVE STRESS LEVELS IN VALPROIC ACID-INDUCED AUTISM

by

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Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disease with a substantially increasing incidence rate. It is mainly characterized by repetitive behavior, intellectual difficulties, social communication and interactions deficits. Many medications, dietary supplements, and behavioral treatments have been recommended for ASD management, however, there is no cure yet. Recent studies have examined the therapeutic potential of the sodium-glucose cotransporter 2 (SGLT2) inhibitors in neurodevelopmental diseases, based on their proved anti-inflammatory and antioxidant effects. The main objective of this study is to assess the ability of canagliflozin in improving the behavioural characteristics of autistic rats and investigate the efficacy of canagliflozin in reducing oxidative stress and acetylcholinesterase activity (AChE) in VPA-exposed rats. Moreover, compare male and female autistic wistar rats with regard to treatment response. ASD was induced by prenatal exposure to 500 mg/kg of Intraperitoneal (i.p.) valproic acid (VPA) at 12.5 gestational day (GD), then autistic rats were treated with 20, 50, or 100 mg/kg of (i.p.) canagliflozin for 29 days. Additionally, rats with VPA-induced ASD were subjected to behavioral assessment at post-natal day 51 (PND) including open field, marble burying, and nestlet shredding tests to examine their repetitive-compulsory behavior and anxiety. After behavioral assessment, rats went through perfusion, and then hippocampus, prefrontal cortex, and cerebellum were extracted to undergo biochemical assays. Canagliflozin achieved substantial ameliorating effects on ASD-like behaviors at various doses. Also, 20, 50, and 100 mg/kg of canagliflozin significantly increased antioxidants levels including GSH, SOD, CAT in different brain regions, as well as decreased MDA and AChE activity in the brain of autistic rats. This study, for the first time, proposed repurposing the use of canagliflozin in ASD management. Moreover, the results stated promising therapeutic effects, that were noticeable in both genders.

Keywords: Autism spectrum disorder, behavioral assessment, biochemical assays, VPA-induced autism, oxidative stress biomarkers