

Section 2: Non-Confidential Abstract

Please provide a scientific abstract of the Project. Clearly state the problem you are trying to solve, your hypothesis and approach, and expected results. **Please Note: This section may be provided to a diverse set of stakeholders including the public.**

Chronic pain complicates many diseases and it is a leading cause of disability for one in five Canadians. Neuropathic pain is among the most debilitating types of chronic pain conditions: it is caused by injury or disease of the nervous system and is stubbornly resistant to the potent pain-relieving effects of opioid medications. An estimated 2 million Canadians and 7% of people worldwide suffer from neuropathic pain. In a struggle to control pain, some people resort to using cannabis. Pain is the most common reason for medical cannabis use, yet the evidence for its effectiveness is not well established. With the recent legalization of cannabis in Canada there is easier access to cannabis and related products. The concern is that people may use cannabis to alleviate pain without adequate consultation with healthcare professionals and without a full understanding of the potential health impact. There is now an urgency to understand the impact of cannabis use on chronic pain.

Here, we address this critical knowledge gap by examining the behavioural and cellular effects of cannabis in a preclinical model of neuropathic pain. We ask whether cannabis alleviates mechanical allodynia, a major symptom of neuropathic pain whereby innocuous stimuli such as gentle touch, elicits pain. Our expert team will determine the impact of cannabis on the progression of this abnormal pain sensitivity, and whether cannabis treatment reverses this pain after it has been established. Using behavioural testing paradigms that model neuropathic pain in people, we will evaluate the potential pain-relieving effects of cannabis. The controlled delivery of commercially available cannabis-derived products allows us to determine with precision the most effective combination of cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC), two active constituents of cannabis. We will also examine the impact of THC and CBD in isolation or in combination with broad-spectrum extracts of cannabis, including terpenes and minor cannabinoids, to evaluate if there is indeed an “entourage effect” of all of the constituents of cannabis versus isolated constituents. Under these conditions, we will discern how cannabis affects the central nervous system, focusing on specialized immune cells that reside within confines of the brain and spinal cord – microglia. These immune cells are targets of cannabinoid drugs and their activity drive change in the nervous system to cause abnormal pain sensitivity. Using advanced cellular imaging, biochemical, genetic, and behavioural approaches, experiments will deconstruct the machinery by which cannabis modulates microglia function and the implications for activity of key pain circuits. This detailed understanding is essential for determining the effectiveness and improving the safety of potential cannabis-based pain therapies.