Hepatic fibrosis, a precursor to cirrhosis, has recently increased incidence. The progression of fibrosis to cirrhosis is a dominant instigator of hepatic failure and liver cancer, thus making the inhibition of this progression a promising treatment option.\(^1\)

There have been two cannabinoid receptors, CB1 and CB2, identified to date. Modulation of these gene protein coupled receptors is known to have psychoactive, inflammatory, and proliferative in humans.\(^2\) These two receptors have been linked to liver fibrosis. The CB1 receptors in the liver enhance the progression of liver disease by promoting fibrinogenesis.\(^3\) The CB2 receptors have been reported to inhibit or reverse fibrinogenesis.\(^4\)

Therapies that target CB1 receptors in the central nervous system (CNS) have adverse mood-related side effects. However, peripherally selective CB1 antagonists provide an alternative strategy that avoids CNS side effects. This study aimed to synthesize peripherally selective CB1 antagonist/CB2 agonist that mitigates hepatic fibrosis and its secondary pathologies.

References