Design and Synthesis of Peripherally Selective CB1 Antagonist/CB2 Agonist to Hinder and Reverse Hepatic Fibrosis

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.

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. These two receptors have been linked to liver fibrosis. The CB1 receptors in the liver enhance the progression of liver disease by promoting fibrinogenesis. The CB2 receptors have been reported to inhibit or reverse fibrinogenesis.

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
