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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 [1].

There have been two cannabinoid receptros, CB1 and CB2, identified to date. Modulation of these gene protein coupled receptors is know to have psychoactive, inflammatory, and proliferative in humans [2]. These two receptors have beenlinked 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 sode effects. This study aimed to synthesize peripherally selective CB1 antagonist/CB2 agonist that mitigates hepatic fibrosis and its secondary pathologies.

References

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