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The Potential for Pharmacokinetic Interactions Between Cannabis Products and Conventional Medications

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Abstract

Purpose: Increased cannabis use and recent drug approvals pose new challenges for avoiding drug interactions between cannabis products and conventional medications. This review aims to identify drug-metabolizing enzymes and drug transporters that are affected by concurrent cannabis use and, conversely, those co-prescribed medications that may alter the exposure to one or more cannabinoids.

Methods: A systematic literature search was conducted utilizing the Google Scholar search engine and MEDLINE (PubMed) database through March 2019. All articles describing in vitro or clinical studies of cannabis drug interaction potential were retrieved for review. Additional articles of interest were obtained through cross-referencing of published bibliographies.

Findings: After comparing the in vitro inhibition parameters to physiologically achievable cannabinoid concentrations, it was concluded that CYP2C9, CYP1A1/2, and CYP1B1 are likely to be inhibited by all 3 major cannabinoids Δ-tetrahydrocannabinol (THC), cannabidiol (CBD), and cannabinol (CBN). The isoforms CYP2D6, CYP2C19, CYP2B6, and CYP2J2 are inhibited by THC and CBD. CYP3A4/5/7 is potentially inhibited by CBD. Δ-Tetrahydrocannabinol also activates CYP2C9 and induces CYP1A1. For non-CYP drug-metabolizing enzymes, UGT1A9 is inhibited by CBD and CBN, whereas UGT2B7 is inhibited by CBD but activated by CBN. Carboxylesterase 1 (CES1) is potentially inhibited by THC and CBD. Clinical studies suggest inhibition of CYP2C19 by CBD, inhibition of CYP2C9 by various cannabis products, and induction of CYP1A2 through cannabis smoking. Evidence of CBD inhibition of UGTs and CES1 has been shown in some studies, but the data are limited at present. We did not identify any clinical studies suggesting an influence of cannabinoids on drug transporters, and in vitro results suggest that a clinical interaction is unlikely.

Conclusions: Medications that are prominent substrates for CYP2C19, CYP2C9, and CYP1A2 may be particularly at risk of altered disposition by concomitant use of cannabis or 1 or more of its constituents. Caution should also be given when coadministered drugs are metabolized by UGT or CES1, on which subject the information remains limited and further investigation is warranted. Conversely, conventional drugs with strong inhibitory or inductive effects on CYP3A4 are expected to affect CBD disposition.

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