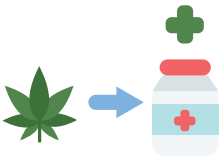
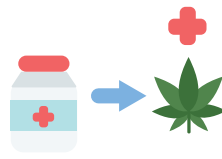


# Selecting Cannabis Products: Drug Interactions



## Cannabinoid levels can be increased by other medications

THC and CBD are metabolized by cytochrome P450 (CYP)3A4. Studies have shown that CYP3A4-inhibitors can nearly double serum levels of both THC and CBD, increasing the psychoactive effects of THC and dose-dependent adverse effects of CBD. Examples of CYP3A4-inhibitors include ketoconazole, macrolides, and verapamil. Similarly, since THC is also metabolized by CYP2C9, a liver enzyme, CYP2C9-inhibitors such as cotrimoxazole, fluoxetine, valproic acid, and amiodarone also increase THC levels and amplify associated effects.



## Cannabinoids can affect levels of other drugs

For example, CBD inhibits CYP2C19, which triples the levels of the active metabolite of clobazam. A similar interaction with other CYP2C19 substrates may also be expected to occur, such as with apripiprazole, citalopram, and diazepam. Additionally, CBD can triple the concentration of tacrolimus, which is a CYP3A4 substrate. Similar interactions with other CYP3A4 substrates may occur, such as alprazolam, carbamazepine, and zopiclone.



## Smoking marijuana can increase clearance of some drugs

Smoked cannabis increases the clearance of drugs metabolized by CYP1A2. In addition to other CYP1A2 substrates such as clozapine and olanzapine, CYP1A2 has been shown to increase clearance of theophylline by nearly 40%. Clearance acceleration has only been demonstrated for regular users (> 2 cigarettes/week).



## Additive effects can occur with other drugs

Additive effects can occur when cannabis is combined with central nervous system (CNS) depressants (e.g. alcohol, opioids), sympathomimetics, and anticholinergics. Caution is recommended if used concomitantly with cannabis, as it can incur adverse effects such as ataxia, drowsiness, tachycardia, confusion, and hypertension.



## There are potential “red flag” interactions

Cannabis may have serious interactions with some drugs. It is recommended that clinicians privilege non-interacting alternatives where clinically feasible. Examples of serious interactions with cannabis include:

- Warfarin: Smoked cannabis may inhibit the metabolism of warfarin (CYP2C9 substrate), resulting in increased international normalized ratio and risk of bleeding.
- Clopidogrel: Since cannabis inhibits CYP2C19, concomitant use leads to subtherapeutic concentrations of clopidogrel. This decreases its protective effects on cardiovascular disease and events.
- Clobazam: Increased risk of benzodiazepine toxicity.
- CNS depressants and sympathomimetics: Additive effects
- Theophylline, clozapine, and olanzapine: Reduced efficiency