Appendix 1 (as supplied by the authors): *Supplemental Table 1: Possible and actual interactions between cannabinoids and other medication*[1-8]

	Tetrahydrocannabinol (THC) **Substrate of CYP3A4 and CYP2C9** **Potential ↑ THC concentration with CYP3A4 and CYP2C9 inhibitors (see below)**	**Cannabidiol (CBD)** **Substrate of CYP3A4 and CYP2C19** **Potential ↑ CBD concentration with CYP3A4 and CYP2C19 inhibitors (see below)**
Pharmacokinetic interactions*		
CYP3A4 inhibitors [e.g.macrolide antibiotics (clarithromycin and erythromycin only), azole antifungals, HIV protease inhibitors, diltiazem, verapamil, amiodarone]	Ketoconazole ↑ THC concentration nearly 2-fold. Similar interaction possible with other 3A4 inhibitors, resulting in enhanced THC psychoactive effects.	Ketoconazole ↑ CBD concentration nearly 2-fold. Similar interaction possible with other 3A4 inhibitors, resulting in enhanced CBD effects, including somnolence and transaminase elevations.
CYP3A4 inducers (e.g. rifamycins, efavirenz, nevirapine, St. John's wort, carbamazepine, phenytoin, phenobarbital)	Rifampin ↓ THC concentration ~ 20%. Similar interaction possible with other 3A4 inducers. Clinical significance unclear.	Rifampin ↓ CBD concentration ~ 60%. Similar interaction possible with other 3A4 inducers. Combined use may decrease effectiveness when used for seizure disorders.
CYP3A4 substrates [e.g. alprazolam, PDE_5 inhibitors (e.g. sildenafil), carbamazepine, HIV protease inhibitors, diltiazem, verapamil, fentanyl, cyclosporine, tacrolimus, sirolimus, simvastatin, atorvastatin, zopiclone)	No effect of THC on CYP3A4 substrates anticipated based on current knowledge.	CBD ↑ tacrolimus concentration 3-fold. Interactions with other 3A4 substrates possible. Monitoring for adverse reactions and/or selecting alternative agents recommended when clinically possible.
CYP2C9 inhibitors e.g. (sulfamethoxazole, amiodarone,	May ↑ THC levels, enhancing psychoactive effects.	No effects anticipated of CYP2C9 inhibitors or inducers based on current knowledge.

Appendix to: Antoniou T, Bodkin J, Ho JMW. Drug interactions with cannabinoids. *CMAJ* 2020. DOI: 10.1503/cmaj.191097.

metronidazole, fluconazole, voriconazole, valproic acid) **CYP2C9 Inducers** (e.g. rifamycins, barbiturates, carbamazepine) **CYP2C9 Substrates** (e.g. warfarin, rosuvastatin, phenytoin)	May ↓ THC levels, attenuating psychoactive effects THC may ↑ levels; monitor for adverse reactions; dose reduction may be required. Cases of increased INR and bleeding with smoked marijuana.	CBD may ↑ levels; monitor for adverse reactions; dose reduction may be required. Cases of increased INR and bleeding with smoked marijuana.
CYP2C19 inhibitors (e.g. cimetidine, omeprazole, esomeprazole, ticlopidine, fluconazole, fluoxetine, isoniazid) **CYP2C19 inducers** (e.g. barbiturates, St. John's wort, carbamazepine, rifamycins) **CYP2C19 substrates** [e.g. aripiprazole, clopidogrel, citalopram, diazepam, N-desmethylclobazam (nCBZ)]	No effects anticipated with 2C19 inhibitors, inducers or substrates, based on currently available knowledge.	Although a CYP2C19 substrate, no impact of omeprazole. Because of potential for interaction, monitor for CBD side effects. Similar effects possible as with 3A4 inducers. CBD ↑ levels of nCBZ 2- to 6-fold. Interactions with other 2C19 substrates possible. Monitor for toxicity. Because clopidogrel is activated by CYP2C19, CBD may compromise antiplatelet activity of this drug.

CYP2B6 substrates (e.g. ,methadone, selegiline, meperidine)	THC may ↑ levels; monitor for adverse reactions; dose reduction may be required.	CBD may ↑ levels; monitor for adverse reactions; dose reduction may be required.
CYP1A2 substrates e.g. (clozapine, theophylline, olanzapine)	Smoked marijuana may ↑ clearance of these drugs. Monitor for loss of efficacy with chronic marijuana use. Conversely, smoking cessation may require dose reductions of 30% and 50% of olanzapine and clozapine, respectively to avoid toxicity.	Smoked marijuana may ↑ clearance of these drugs. Monitor for loss of efficacy with chronic marijuana use. Conversely, smoking cessation may require dose reductions of 30% and 50% of olanzapine and clozapine, respectively to avoid toxicity.
P-glycoprotein substrates Substantial overlap with CYP3A4 substrates, and also includes dabigatran etexilate, digoxin and loperamide.	No effect of THC on p-glycoprotein substrates anticipated.	CBD may inhibit p-glycoprotein drug transport. Monitor for increased toxicity of substrates.
Pharmacodynamic interactions		
Central nervous system depressants** (e.g. alcohol, opioids, benzodiazepine receptor agonists, tricyclic antidepressants)	Additive cognitive and psychomotor impairment.	Additive cognitive and psychomotor impairment.
Sympathomimetics (e.g. amphetamines, cocaine, noradrenergic and anticholinergic agents)	Additive tachycardia, hypertension and fluid retention.	No interaction anticipated.

*List of substrates, inhibitors and inducers are representative only, and not exhaustive.

** Increased risk among individuals with cognitive impairment or advanced age.

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