

Supplementary

**Predicting the potential for cannabinoids to precipitate pharmacokinetic drug interactions via reversible inhibition or inactivation
of major cytochromes P450**

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Supplementary Table 1. f_m , F_g , and K_{deg} values used in mechanistic static modeling of drug interactions

Object Drug	Enzyme	f_m	F_g	$K_{deg} (\text{min}^{-1})$
Theophylline	CYP1A2	0.75 (Theophylline Package Insert; Zhou <i>et al.</i> , 2018)	-	0.00031 ^a (Faber and Fuhr, 2004; Xu <i>et al.</i> , 2015)
Diclofenac	CYP2C9	0.98 (Bort <i>et al.</i> , 1999; Zhou <i>et al.</i> , 2018)	0.64 (Varma <i>et al.</i> , 2009)	-
Omeprazole	CYP2C19	0.87 (Obach <i>et al.</i> , 2006)	-	0.00045 ^a (Ghanbari <i>et al.</i> , 2006; Shirasaka <i>et al.</i> , 2013)
Dextromethorphan	CYP2D6	1.00 (Obach <i>et al.</i> , 2006)	-	-
Midazolam	CYP3A4	0.75 (Parmentier <i>et al.</i> , 2017)	0.55 (Varma <i>et al.</i> , 2009)	0.00032 ^a , 0.00048 ^b (Fahmi <i>et al.</i> , 2008; Xu <i>et al.</i> , 2015)

^a K_{deg} in the liver, ^b K_{deg} in the intestine

Supplementary Table 2. Low, high, and maximum^a oral doses of CBD used for medicinal purposes^b

Route of Administration	Low Dose (≤ 200 mg)			High Dose (> 200 mg)		
	Type	Dose (mg)	Reference	Type	Dose (mg)	Reference
Oral	Prescription	24	(Shannon and Opila-Lehman, 2016)	Prescription	268	(Crippa <i>et al.</i> , 2011)
	Prescription	50	(Chagas <i>et al.</i> , 2014)	Prescription	400	(Devinsky <i>et al.</i> , 2018)
	Prescription	68	(Consroe <i>et al.</i> , 1991)	Prescription	532	(Leweke <i>et al.</i> , 2012)
	Prescription	80	(Rosenberg <i>et al.</i> , 2017)	Prescription	640	(Zuardi <i>et al.</i> , 2006)
	Prescription	100	(Snider and Consroe, 1984)	Prescription	668	(McGuire <i>et al.</i> , 2018)
	Prescription	132	(Jadoon <i>et al.</i> , 2016)	Prescription	800	(Epidiolex® Package Insert)
				Prescription	1000	(Kaplan <i>et al.</i> , 2017)
	Prescription	200	(Chagas <i>et al.</i> , 2014)	Prescription	2000	(Devinsky <i>et al.</i> , 2016; Hess <i>et al.</i> , 2016; Rosenberg <i>et al.</i> , 2017; Warren <i>et al.</i> , 2017)
	OTC	5	(https://cbdoilreview.org/cbd-cannabidiol/cbd-dosage)			
	OTC	20	OTC	300	(Amazon.com)	
	OTC	30	OTC	350	(https://cbdoilreview.org/cbd-cannabidiol/cbd-dosage)	
	OTC	50	OTC	640		
Average Dose		69			691	

^aThe maximum single oral dose of CBD tested in clinical studies is 2,000 mg (Devinsky *et al.*, 2016; Hess *et al.*, 2016; Rosenberg *et al.*, 2017; Warren *et al.*, 2017).

^bThese doses are per single dose of CBD. When used for medicinal purposes, the listed CBD dose is usually administered twice a day.

Supplementary Table 3. Low, high, and maximum^a oral and inhaled doses of THC used for recreational and medicinal purposes^b

Route of Administration	Low Dose (≤ 50 mg)			High Dose (> 50 mg)		
	Use	Dose (mg)	Reference	Use	Dose (mg)	Reference
Oral	Medicinal	8	(de Vries <i>et al.</i> , 2016, 2017)	Recreational	100	(Sulak, 2018)
	Medicinal	10	(Marinol® Package Insert)	Medicinal	156	(Ware <i>et al.</i> , 2015)
	Medicinal	15	(Childs <i>et al.</i> , 2017)			
	Medicinal	30	(Kahan <i>et al.</i> , 2014)			
	Recreational	2.5	(Sulak, 2018)			
	Recreational	50	(Sulak, 2018)			
Average Oral Dose		18			128	
Inhalation	Medicinal	6	(Klumpers <i>et al.</i> , 2012)	Medicinal	53	(Lee <i>et al.</i> , 2015)
	Medicinal	8	(Solowij <i>et al.</i> , 2019)	Medicinal	54	(Schwone <i>et al.</i> , 2011)
	Medicinal	9	(Ohlsson <i>et al.</i> , 1986)	Medicinal	70	(Kahan <i>et al.</i> , 2014)
	Medicinal	25	(Kahan <i>et al.</i> , 2014; Spindle <i>et al.</i> , 2018)	Medicinal	72	(Ellis <i>et al.</i> , 2009)
	Medicinal	32	(Abrams <i>et al.</i> , 2007)	Medicinal	78	(Ware <i>et al.</i> , 2015)
	Medicinal	34	(Huestis <i>et al.</i> , 1992; Wilsey <i>et al.</i> , 2008)	Recreational	100	(keytocannabis.com)
	Medicinal	53	(Lee <i>et al.</i> , 2015)			
	Medicinal	54	(Schwone <i>et al.</i> , 2011)			
	Recreational	30	(Barreda <i>et al.</i> , 2018)			
Average Inhaled Dose		26			71	

^aThe maximum single oral dose of THC tested in a clinical study is 156 mg and inhaled dose for recreational use is 100 mg, respectively (Ware *et al.*, 2015 and keytocannabis.com)

^bThese doses are per single dose of THC. When used for medicinal purposes, the listed THC dose is usually administered twice a day orally and 4 times a day by inhalation.

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