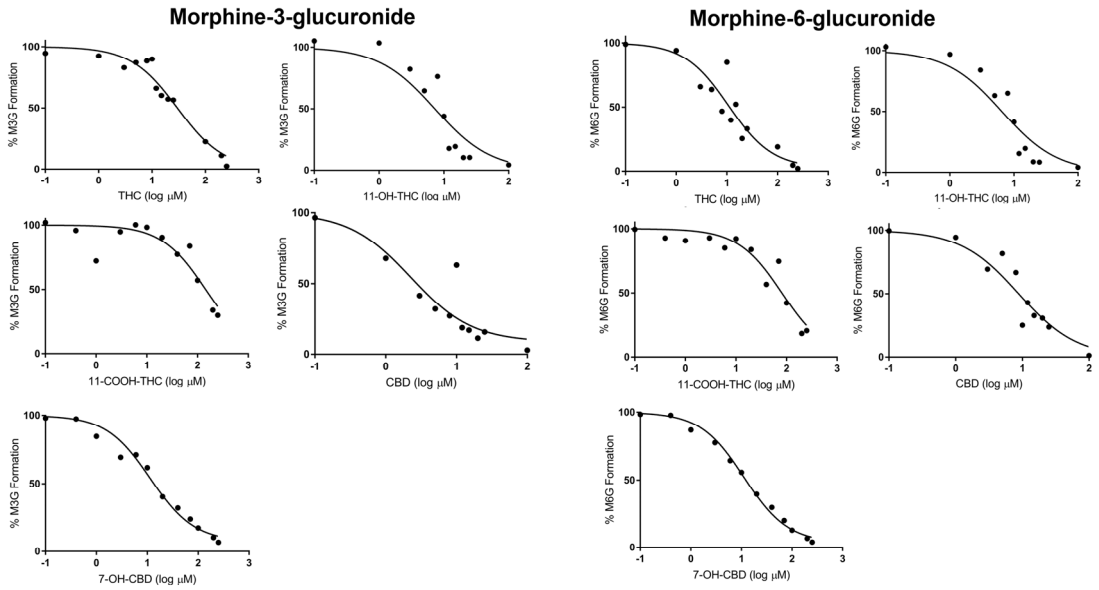

Figure S1: Representative IC_{50} curves in HLM against morphine-3-glucuronide and morphine-6-glucuronide formation

Table S1. Estimated maximum plasma concentrations of THC and CBD and their metabolites used to predict the magnitude of *in vivo* cannabinoid – drug interactions after consumption of cannabis by either oral or inhalation route.

Cannabinoid	Dose (mg)[a]	Route of Administration	$C_{max,hepatic\ inlet,u}$ (μM)
THC	20	Oral	0.03
	130	Oral	0.20
	160	Oral	0.24
	25	Inhalation	0.25
	70	Inhalation	0.69
	100	Inhalation	0.99
11-OH-THC	20	Oral	0.02
	130	Oral	0.10
	160	Oral	0.12
	25	Inhalation	0.01
	70	Inhalation	0.03
	100	Inhalation	0.05
11-COOH-THC	20	Oral	0.19
	130	Oral	1.22
	160	Oral	1.50
	25	Inhalation	0.07
	70	Inhalation	0.18
	100	Inhalation	0.26
CBD	70	Oral	0.09
	700	Oral	0.89
	2000	Oral	2.54
	19	Inhalation	0.35[c]
7-OH-CBD	70	Oral	0.03
	700	Oral	0.34

	2000	Oral	0.98
	19	Inhalation	N.D.[b]

[a] Doses and C_{max} used to predict AUCR were reported from Bansal et al., 2022 [56]. Doses used for modeling 11-OH-THC and 7-OH-CBD were from administered doses of THC and CBD, respectively. $C_{max,hepatic\ inlet,u} = f_{u,p} \times \left(C_{max} + \frac{F_a \times F_g \times K_a \times Dose}{Q_h \times R_b}\right)$, where $f_{u,P}$ (unbound fraction in plasma) was set to 0.03 (Garrett and Hunt, 1974) [52], F_a (fraction absorbed) and F_g (dose that escapes gut metabolism) for THC and CBD were set to 1 (FDA Drug Interactions Guidance, 2020) [53], k_a for both THC and CBD was set to 0.02 (Cox et al., 2019) [45], Q_H (hepatic blood flow) – 1500 mL/min, and BP (blood to plasma ratio) for THC and CBD was set to 0.4 (Schwilke et al., 2009) [55]. [b] N.D., not determined. [c] Doses and C_{max} used to predict AUCR were reported from Cox et al., 2019 [45].