Table 1
Relationships between plant neurotoxins commonly used as drugs and CNS receptors.

Drug	Plant	Toxin	Neurotransmitter	Receptor
Tobacco, Pituri	*Nicotiana, Duboisia*	Nicotine[a]	Acetylcholine	Nicotinic receptor
Betel nut	*Areca catechu*	Arecoline[a]	Acetylcholine	Muscarinic receptor
Coca	*Erythroxylum*	Cocaine[c]	Norepinephrine, epinephrine	Adrenergic receptors
Khat	*Catha edulis*	Ephedrine[c], cathinone[a,c]	Norepinephrine, epinephrine	Adrenergic receptors
Coca	*Erythroxylum*	Cocaine[c]	Dopamine	Dopamine receptor
Khat	*Catha edulis*	Cathinone[a,c]	Dopamine	Dopamine receptor
Coffee, Cola nut	*Coffea, Cola nitida*	Caffeine[b]	Adenosine	Adenosine receptor
Tea	*Camellia sinensis*	Caffeine[b], theophylline[b], theobromine[b]	Adenosine	Adenosine receptor
Chocolate	*Theobromine cacao*	Theobromine[b]	Adenosine	Adenosine receptor
Opium	*Papaver somniferum*	Codeine[a], morphine[a]	Endorphins	Opioid receptor
Cannabis	*Cannabis sativa*	Δ9-THC[a]	Anandamide	Cannabinoid receptor

[a]receptor agonist, [b]receptor antagonist, [c]reuptake inhibitor

Table 2

Human cytochrome P450 natural substrates and enzyme kinetics constants. V_{max} is the maximum reaction rate per unit enzyme. K_m, the Michaelis-Menten constant, is the substrate concentration at which the reaction rate = $V_{max}/2$ (lower values indicate higher enzyme affinity for substrate). V_{max} / K_m is an index of enzyme activity (higher values indicate higher enzyme activity). Kinetic values can vary widely; values here are representative of one metabolic pathway (substrates are typically metabolized via multiple pathways). Plants listed are often not the exclusive source of the neurotoxin.

Enzyme/substrates	Xenobiotic and endogenous sources	$K_m (\mu M)$	V_{max}	V_{max} / K_m
CYP1A2				
Caffeine	Plant neurotoxin (*Coffea* – coffee)	460	570[b]	1.24
Theophylline	Plant neurotoxin (*Camellia sinensis* – tea)	310	43.3[b]	0.14
Theobromine	Plant neurotoxin (*Theobromine cacao* – chocolate)	2580	1720[b]	0.67
Aflatoxin B1	Fungus neurotoxin	36	0.92[a]	0.026
PhIP	Cooked meat	46	1.79[a]	0.039
Estradiol	Sex hormone	27.5	17.4[a]	0.63
Melatonin	Hormone	25.9	10.6[a]	0.41
CYP2A6				
Nicotine	Plant neurotoxin (*Nicotiana* – tobacco)	95.3	154.1[b]	1.69
Coumarin	Plant neurotoxin (*Dipteryx odorata* – tonka bean)	0.6	0.6[a]	1.0
Cotinine	Nicotine metabolite	234.5	37.2[b]	0.16
CYP2B6				
Nicotine	Plant neurotoxin [induces 2B6 in the brain]			
Diazepam	Synthetic drug; trace amounts in plants	181	8.5[a]	0.05
CYP2C8				
Taxol	Plant neurotoxin (*Taxus brevifolia*)	5.4	30[a]	5.6
Arachidonic acid	Essential omega-6 fatty acid	71	0.078[a]	0.001
Retinol	Vitamin A	50	1.2[a]	0.024
CYP2C9				
Δ9-THC	Plant neurotoxin (*Cannabis sativa* – marijuana)	2.1	6.4[a]	3.0
CYP2C19				
Melatonin	Hormone	282.2		
Progesterone	Hormone	3.6	1.4[a]	0.39
CYP2D6				
Codeine	Plant neurotoxin (*Papaver somniferum* – opium poppy)	190	6.4[a]	0.034
Harmaline	Plant neurotoxin (*Peganum harmala*)	1.41	39.9[a]	28.3
Harmine	Plant neurotoxin (*Peganum harmala*)	7.42	29.7[a]	4.0
Sparteine	Plant neurotoxin (*Lupinus*)	44		
Yohimbine	Plant neurotoxin (*Pausinystalia yohimbe*)	2.0	147.4[b]	75.5
CYP2E1				
Theobromine	Plant neurotoxin (*Theobromine cacao* – chocolate)	3400		
Ethanol	Yeast waste product	23400	23.2[a]	0.001
CYP3A4				
Cocaine	Plant neurotoxin (*Erythroxylum coca*)	2700	3744.4[b]	1.4
Quinine	Plant neurotoxin (*Cinchona*)	106	1330[b]	13
Aflatoxin B1	Fungus neurotoxin	139	61[a]	0.45
Testosterone	Hormone	52	5400[b]	101
Cortisol	Hormone	15	6.4[b]	0.42

[a] *pmol/min/pmol* P450; [b] *pmol/min/mg* microsomal protein

Data from Bland, Haining, Tracy, and Callery (2005); Bu (2006); Gates and Miners (1999); Ladona, Gonzalez, Rane, Peter, and Torre (2000); Le Corre et al. (2004); Lewis (2001, 2003); Osikowska-Evers and Eichelbaum (1986); Projean, Morin, Tu, and Ducharme (2003); Yang et al. (1998); Yu, Kneller, Rettie, and Haining (2002); Yu, Idle, Krausz, Kupfer, and Gonzalez (2003); Ma, Idle, Krausz, and Gonzalez (2005); Usmani, Cho, Rose, and Hodgson (2006); Yamazaki and Shimada (1997); Bloomer, Clarke, and Chenery (1995); Murphy, Raulinaitis, and Brown (2005); Hammons et al. (1997); Nakajima et al. (1996, 1996); Tjia, Colbert, and Back (1996); Ha, Follath, Chen, and Krähenbühl (1996); Asai, Imaoka, Kuroki, Monna, and Funae (1996); Marill, Cresteil, Lanotte, and Chabot (2000); Rahman, Korzekwa, Grogan, Gonzalez, and Harris (1994); Campbell, Grant, Inaba, and Kalow (1987); Gallagher, Kunze, Stapleton, and Eaton (1996).

Table 3

Example ethnic population frequencies of CYP2A6 and CYP2D6 alleles with known in vivo *enzyme activity. Frequencies compiled from different studies in the same ethnic population are only approximately comparable.*

Allele	Enzyme activity	Population frequencies (%)				
		Ghanaian[1]	Caucasian[2,3]	Chinese[1,2,3]	Japanese[1,2,3,4]	
CYP2A6*1A/B	Normal	91.9	88.4	61.7	48.3	
CYP2A6*2	None	0	2.3	0	0	
CYP2A6*4	None	1.9	1.2	15.1	20.1	
CYP2A6*5	None	0	0	1	0	
CYP2A6*7	Reduced	0	0	2.2	6.5	
CYP2A6*9	Reduced	5.7	5.2	15.7	21.3	
CYP2A6*10	Reduced	0	0	0.4	1.1	
CYP2A6*12	Reduced		3	0	0	
		Black African[5]	Caucasian[5]	Asian[5]	Ethiopian[6]	Saudi Arabian[7]
CYP2D6*2xn	Increased	2	1-5	0-2	16.0	10.4
CYP2D6*4	None	2	12-21	1	1.2	3.5
CYP2D6*5	None	4	2-7	6	3.3	1.0
CYP2D6*10	Reduced	6	1-2	51	8.6	3.0
CYP2D6*17	Reduced*	20-35	0	0	9.0	3.0

1: Gyamfi, Fujieda, Kiyotani, Yamazaki, and Kamataki (2005); 2: Nakajima, Kuroiwa, and Yokoi (2002); 3: Haberl et al. (2005); 4: Yoshida et al. (2003); 5: Ingelman-Sundberg (2005); 6: Aklillu et al. (1996); 7: McLellan, Oscarson, Seidegård, Evans, and Ingelman-Sundberg (1997)

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