Pharmacodynamic and Pharmacokinetic Properties of Commonly Prescribed Opioids

Hydroxylated phenanthrene		Receptor binding	Mu Receptor binding affinity	Equivalent doses	$T_{1/2}$	Duration of Action	Volume of Distribution (Vd)	Metabolism	Available Doses[€]
Morphine (Brand names: MSIR, Roxanol, MSContin, Avinza, Kadian)		Binds to both μ1 & μ2 ~equally Weak κ agonist M-6-G δ-receptor agonist	+	30mg PO	2-4hrs	IR: 4 hrs	3-4 L/kg	Phase II glucuronidation to morphine-3-glucuronide (not active for analgesia but will cause side effects) and morphine-6-glucuronide (active) Both major metabolites accumulate in renal failure Morphine (parent) accumulates in hepatic failure	IV: 2mg/ml, 4mg/ml, 5mg/ml,8mg/ml, 10mg/0.7ml, 10mg/ml, 15mg/ml, 25mg/ml, 50mg/ml IR: 15mg,30mg Solution: 2mg/ml, 4mg/ml, 20mg/ml SA: MSContin – 15mg, 30mg, 60mg, 100mg, 200mg; Avinza – 30mg, 60mg, 90mg, 120mg; Kadian – 20mg, 30mg, 50mg, 60mg, 80mg, 100mg, 200mg
Codeine		Prodrug, metabolized to morphine μ-receptor agonist with low binding affinity	+/- Metabolites responsible for analgesic properties	200mg po	2.5-3.5hrs	4-6 hrs	3.5 L/kg	2D6 mediated O-demethylation to morphine (active) Phase II glucuronidation to codeine-6-glucuronide 3A4 mediated N-demethylation to norcodeine (inactive)	IV: 15mg/ml, 30mg/ml IR: phosphate – 30mg, 60mg; sulfate – 15mg, 30mg, 60mg SA: (not available in US) 50mg, 100mg, 150mg, 200mg
Diacetyl-morphine		Not Available	Not Available	Not Available	3-5 min	Not available	60-100L	Peripheral Metabolism to 6-acetylmorphine, Morphine, Morphine-3-glucuronide, Normorphine, 6-acetylmorphine 3-glucuronide, Normorphine glucuronide	Not available in the US

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Dehydroxylated phenanthrene		Receptor binding	Mu Receptor binding affinity	Equivalent doses	$T_{1/2}$	Duration of Action	Volume of Distribution (Vd)	Metabolism	Available Doses[€]
Levorphanol (Brand name: Levo-Dromoran)		μ-agonist κ1, κ3 >>κ2 Non-competitive NMDA receptor antagonist SNRI activity	++	4mg	~30 hrs	6-15 hrs	10-13 L/kg	Phase II glucuronidation to levorphanol-3-glucuronide	IV – 2mg/ml IR – 1mg, 2mg, 3mg
Hydromorphone (Brand name: Dilaudid)		μ receptor agonist	++	7.5mg PO	1-3 hrs	IR: 4-5 hrs	4 L/kg	Phase II glucuronidation to hydromorphone-3-glucuronide and to some extent hydromorphone-6-glucuronide H3G accumulates in renal failure	IV: 1mg/ml, 2mg/ml, 4mg/ml, 10mg/ml IR: 2mg, 4mg, 8mg
Hydrocodone (Brand names: Vicodin, Lortab, Lorcet, Vicoprofen)		μ receptor agonist with low binding affinity	+	30mg PO	3.8 hrs	4-6 hrs	3.4-4.7 L/kg	O-demethylation, N-demethylation and 6-keto reduction to 6-α- and 6-β-hydroxymetabolites	Combination with APAP 2.5/500mg, 5/325mg, 7.5/325mg, 10/325mg, 5/500mg, 7.5/500mg, 10/500mg, 7.5/750mg, 10/650mg, 10/660mg Combination with IBU 5/200mg, 7.5/200mg
Oxycodone (Brand names: Oxy IR, Oxycontin, Roxicodone, Percocet, Roxicet, Tylox)		μ receptor agonist with low binding affinity	+	20mg PO	IR: 2-3 hrs SA: ~5 hrs	IR: 3-6 hrs SA: 12 hrs	2.6 L/kg	*3A4 mediated N-demethylation to noroxycodone *2D6 mediated O-demethylation to oxymorphone (active)	IR: 5mg, 15mg, 30mg Solution: 1mg/ml, 20mg/ml SA: 10mg, 20mg, 40mg, 60mg, 80mg, 160mg Combination with APAP: 5/325mg, 5/500mg, 7.5/325mg, 7.5/500mg, 10/325mg, 10/350mg
Oxymorphone (Brand name: Opana, Opana ER)		μ receptor agonist with low binding affinity	*	10mg PO	IV: 2 hrs IR:7-9 hrs SA:9-11 hrs	IV: 3-6 hrs IR: 4-6hrs SA: ~12 hrs	1.9-4.2 L/kg	Phase II glucuronidation to oxymorphone-3-glucuronide	IV: 1mg/ml IR: 5mg, 10mg SA: 5mg, 10mg, 20mg, 40mg
Buprenorphine (Brand names: Buprenex Buprenex Subutex, Suboxone)		Binds to μ1>>>>μ2 ~90% more doesn't block the alpha receptor† as much as morphine • means no withdrawal • not addicting κ receptor antagonist	++++	0.3mg IV	2.2 hrs	6-8 hrs	97-187 L/kg	3A4 mediated N-dealkylation to norbuprenorphine (weakly active) Phase II glucuronidation of both the parent compound and norbuprenorphine	IV/IM – 0.3mg/ml SL – 2mg, 8mg SL combination with naltrexone-2mg/0.5mg, 8mg/2mg

Phenylpiperidine		Receptor binding	Mu Receptor binding affinity	Equivalent doses	$T_{1/2}$	Duration of Action	Volume of Distribution (Vd)	Metabolism	Available Doses[€]
Fentanyl (Brand names: Sublimaze, Actiq, Duragesic)		μ receptor agonist	+++	0.1mg IV/IM	IV: 2-4 hrs Transdermal patch: 17-22 hrs Transmucosal lozenge: 7hrs	IV: 0.5-1 hr IM:1-2 hrs Transdermal: 48-72 hours	6 L/kg	3A4 mediated oxidative N-dealkylation to norfentanyl	IV:0.05mg/ml Transdermal patch: 12mcg/hr, 25mcg/hr, 50mcg/hr, 75mcg/hr, 100mcg/hr Transmucosal Lozenge: 200mcg, 400mcg, 600mcg, 800mcg, 1200mcg, 1600mcg
Meperidine (Brand name: Demerol)		μ receptor agonist δ receptor agonist	**	200mg PO	Parent : 2.5-4 hrs Liver Disease – 7-11 hrs Normeperidine: 15-30 hrs	2-5 hrs	3.7 L/kg	Phase II hydrolysis to meperidinic acid N-demethylation to normeperidine (neurotoxic) normeperidine accumulates in	IM/SC: 25mg/ml, 50mg/ml, 75mg/ml, 100mg/ml Solution/Syrup: 10mg/ml IR: 50mg, 100mg
Diphenylheptanes		Receptor binding	Mu Receptor binding affinity	Equivalent doses	$T_{1/2}$	Duration of Action	Volume of Distribution (Vd)	Metabolism	Available Doses[€]
Proproxyphene (Brand names: Darvon, Darvon-N, Darvon Compound 32, Darvon Compound 65, Darvocet A, Darvocet N)		μ receptor agonist	++	130mg * or 200mg** PO *HCl salt **napsylate salt	Parent: 6-12 hrs Norproproxyphene – 30-36 hrs	4-6 hrs	16 L/kg	3A4 mediated N-demethylation to norproproxyphene with is excreted by the kidneys *metabolite accumulates in renal failure	IR: 65mg, 100mg Combo with APAP: 50/325mg, 65/650mg, 100/325mg, 100/650mg
Methadone (Brand name: Dolophine, Methadose)		μ receptor agonist Non-competitive NMDA receptor antagonist SNRI activity	++	7.5 mg PO	8-59 hrs	4-8 hrs	Vd_{ss}-1-8 L/kg	3A4, 2B6, 2C19 mediated N-demethylation to 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidene (EDDP)	IV/IM: 10mg/ml Solution: 1mg/ml, 2mg/ml, 10mg/ml Tablets: 5mg, 10mg
Analgesic - Miscellaneous									
Tapentadol (Brand name: Nucynta)		μ-receptor agonist with low binding affinity NRI activity	- *18x less potent than morphine	75-100mg	4 hrs	4-6 hrs	540 ± 98 L	Phase II glucuronidation to O-glucuronide 2C9/2C19 mediated methylation to N-desmethyl-tapentadol	50mg, 75mg, 100mg

[€]Most common dosage forms listed; not all inclusive

†Alpha receptor stimulation = withdrawal symptoms. Since alpha-receptor sits relatively close to the μ-receptor it gets blocked by the morphine molecule when morphine interacts with the μ-receptor, without MS then receptor is available for interactions.

‡Equianalgesic conversions with methadone are difficult due to the variable half-life of methadone.