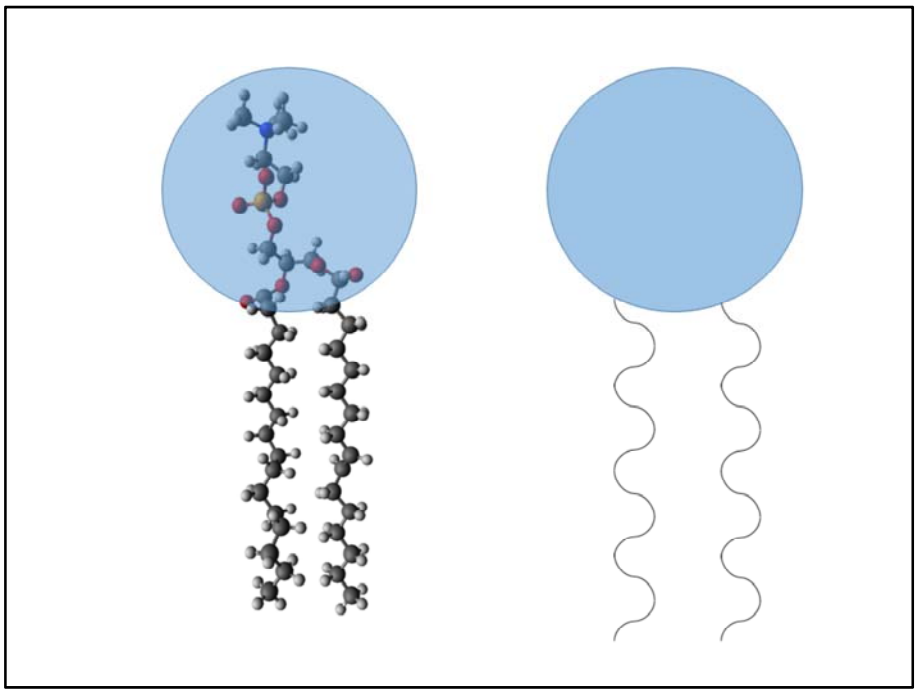
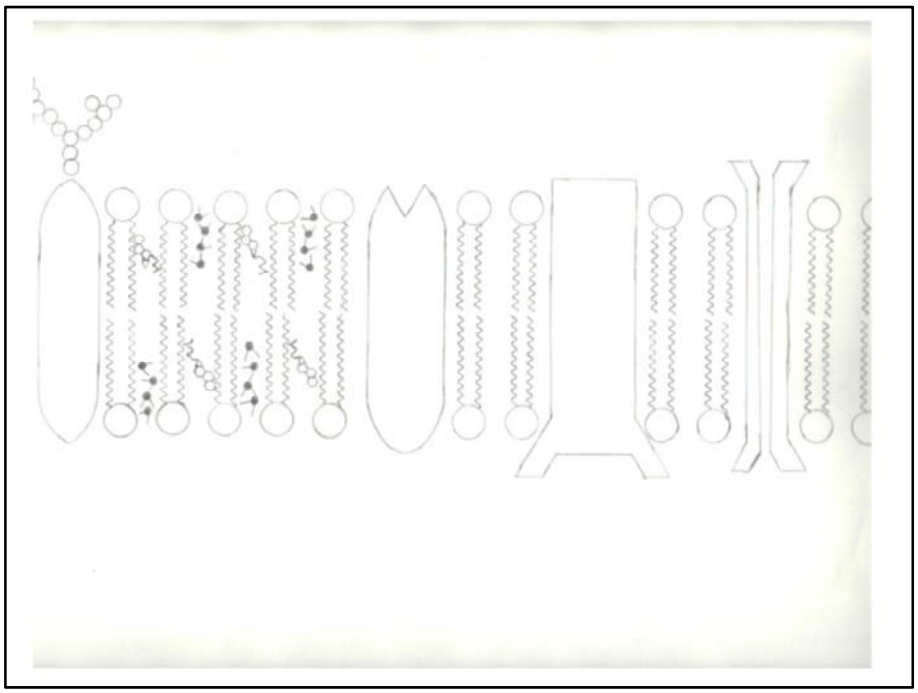
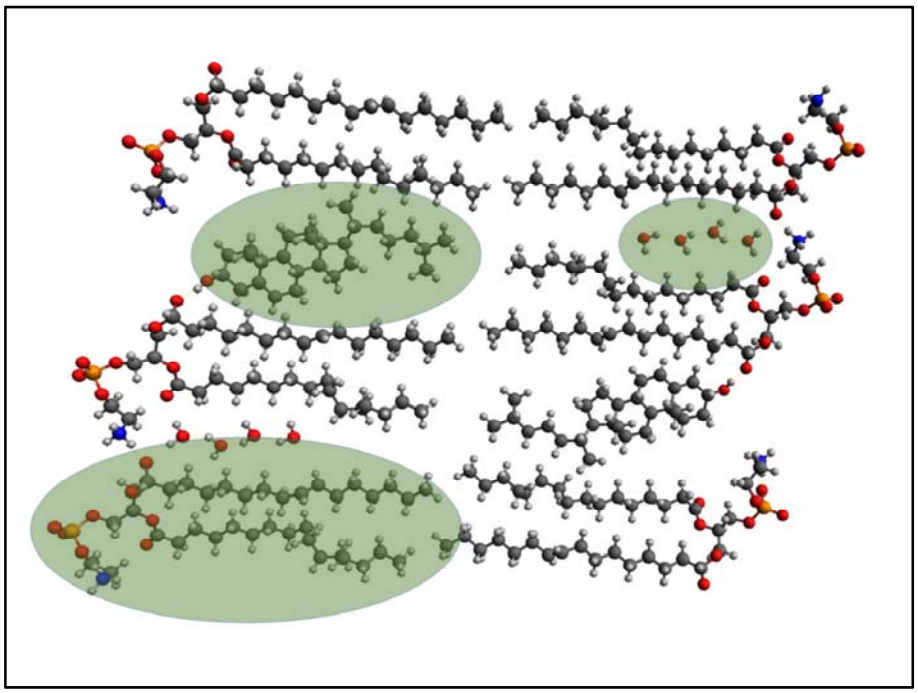
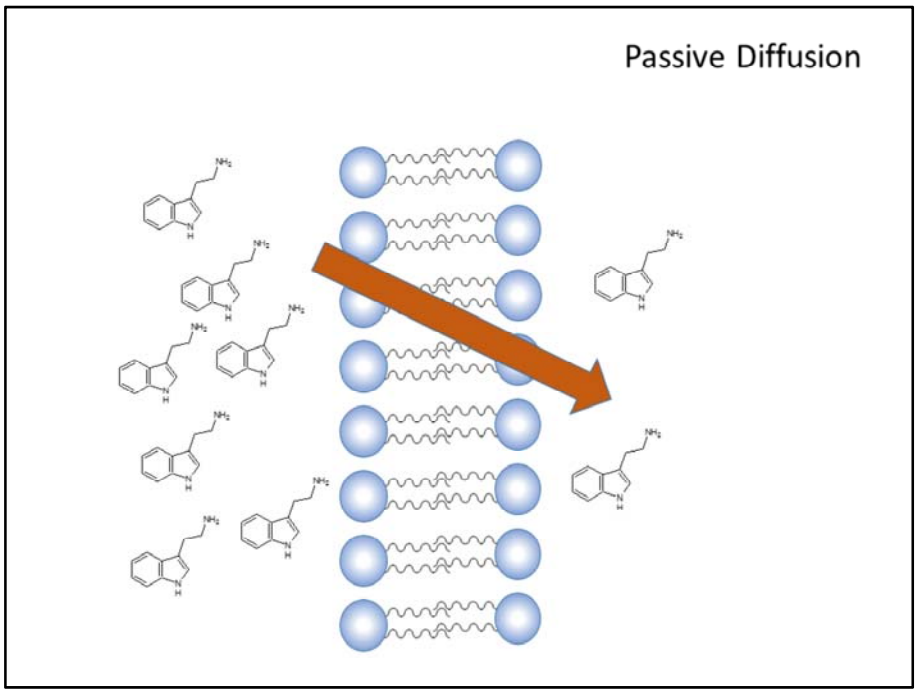
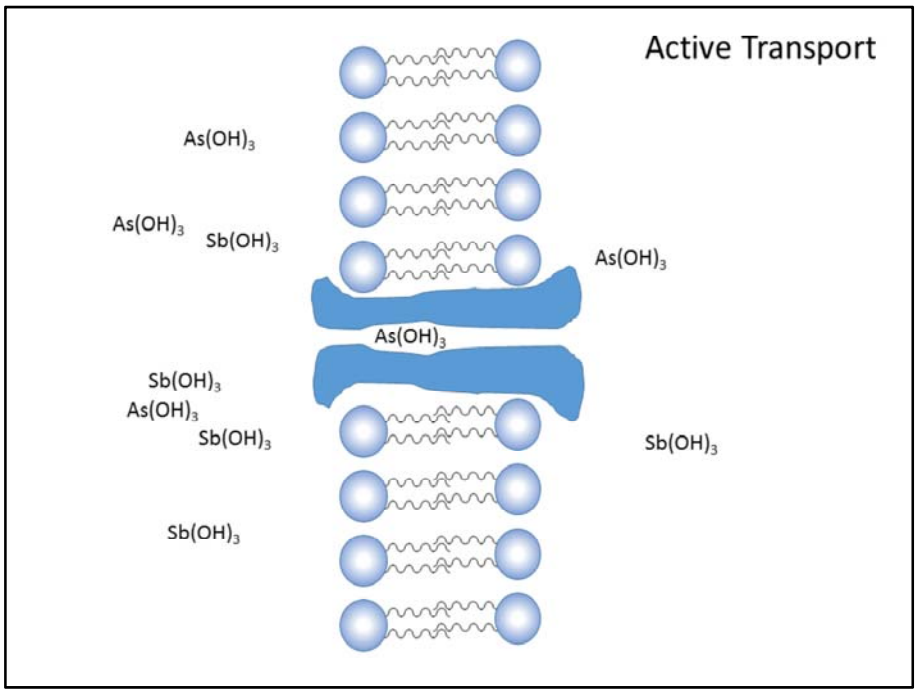
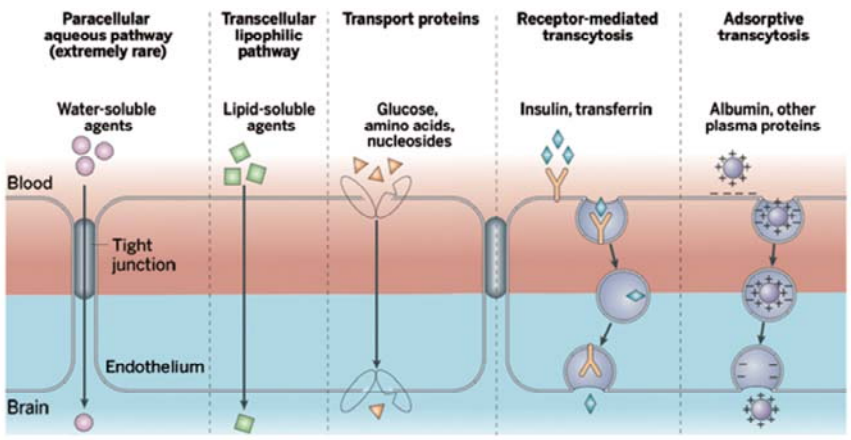







Passive Diffusion


Active Transport
As(OH)3
As(OH)3
Sb(OH)3
As(OH)3
As(OH)3
Sb(OH)3
As(OH)3
Sb(OH)3
Sb(OH)3
Sb(OH)3



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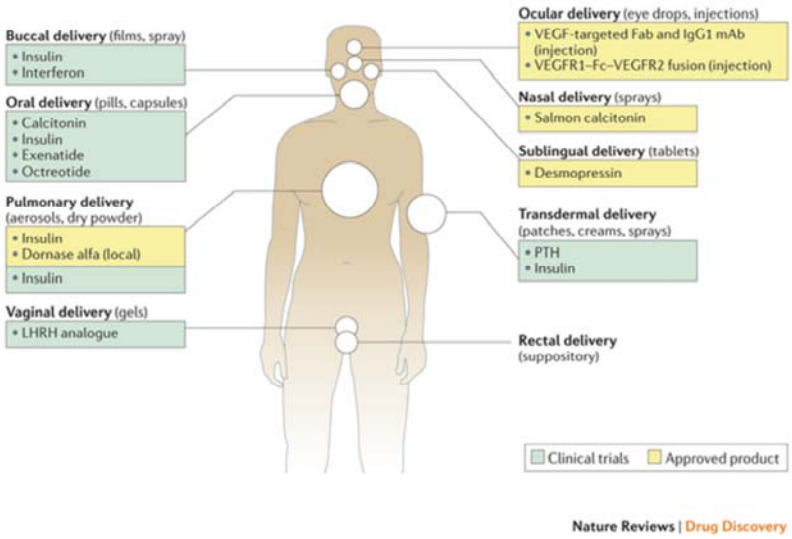


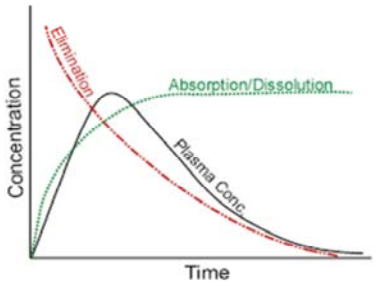
Nature Reviews Drug Discovery 13, 655–672 (2014) doi:10.1038/nrd4363

Bioavailability

Examples of <100% Availability

- Incomplete absorption
- Decomposition
- First-pass metabolic inactivation
- Poor transport

$$Absolute\ bioavailability\ (F) = \frac{AUC_{\ po}}{AUC_{\ iv}} \times \frac{Dose_{iv}}{Dose_{po}} \times 100$$

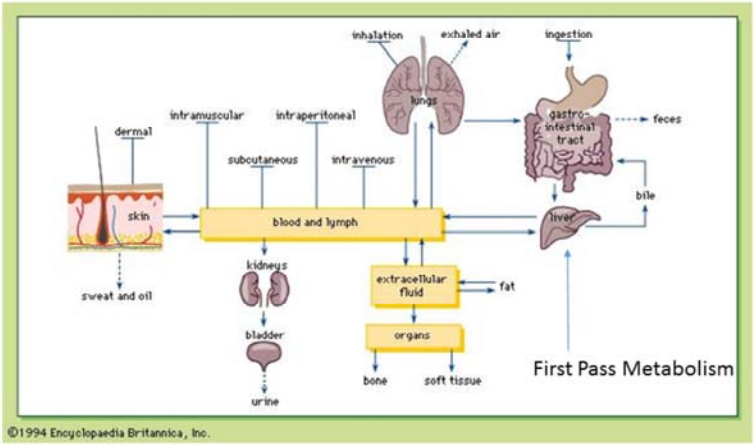


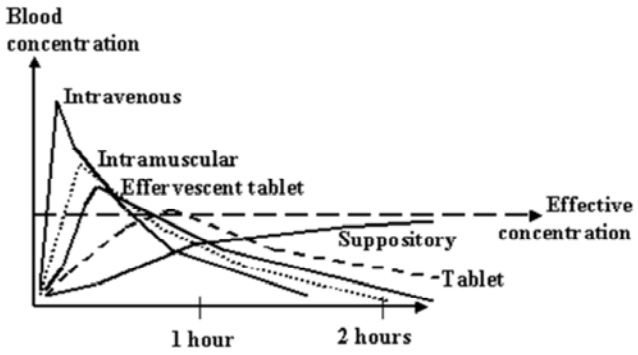
Bioavailability

$$Relative\ bioavailability\ (F) = \frac{AUC_{\ po}(test)}{AUC_{\ po}(std)} \times \frac{Dose_{po}(std)}{Dose_{po}(test)} \times 100$$

Method of Entry:

1. Pulmonary (High Surface area – Many Capillaries)
2. Gastrointestinal
3. Dermal
4. IV
5. Muscle Injection





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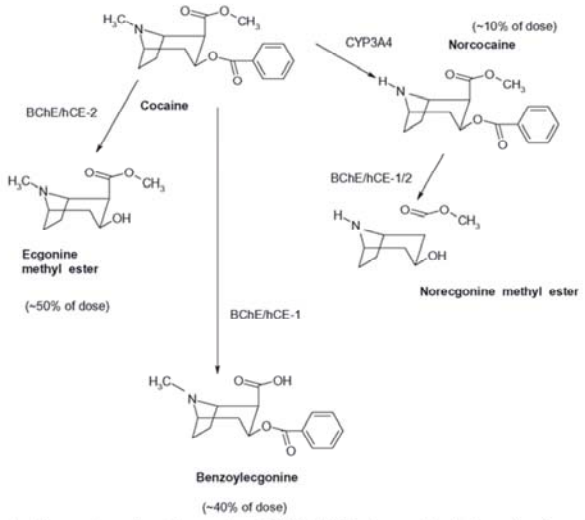
Cocaine (Metabolism of Major Illicit Drugs) (Human Drug Metabolism)
http://what-when-how.com/human-drug-metabolism/cocaine-metabolism-of-major-illicit-drugs-human-drug-metabolism/



Cocaine metabolism, showing the role of CYP3A4 in demethylation (toxic pathway) and human carboxylesterases (hCE-1 and 2) and butyrylcholinesterase (BChE). Esterases are found in virtually every tissue, clearing cocaine extremely rapidly.

Drug	Dose (mg)	half-life (h)	Bioavalability			Source
			Nasal	Smoking	Oral	
Heroin		0.1				NHTSA
Acetylsalicylic Acid		0.25				PfC
GHB	2000-4000	0.5				NHTSA
Cocaine	40-100	0.8	57%	70%		NHTSA
Morphine	5-30	1.9			30%	PfC
Acetaminophen		2				PfC
Ketamine		2.3	40%		20%	NHTSA
LSD		3				NHTSA
Oxycodone	2.5-30	5				NDAA
MDMA		7				NHTSA
Caffeine		8				NDAA
Methamphetamines	2.5-15	10.1				NHTSA
PCP		21		50%		NHTSA
Methadone	20-200	40			75%	NHTSA
Diazepam	4-40	43			99%	NHTSA
THC	2.5-10	72				NHTSA
Phenobarbital		100				NDAA

Clearance:

$$CL_{system} = CL_{renal} + CL_{hepatic} + CL_{excretion} + CL_{other}$$

$$CL_{renal} = \frac{C_{urinary} * V_{urinary}}{C_{plasma}}$$

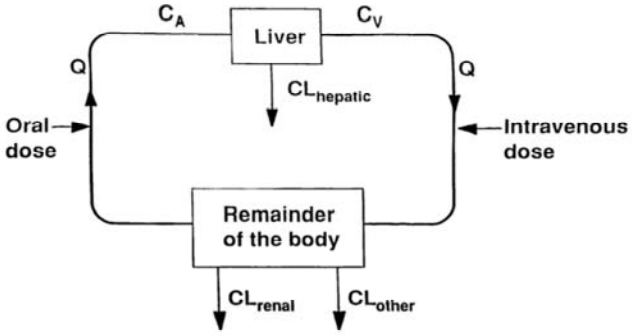


FIG. 1.—A schematic representation of the concentration–clearance relationship.

Benet, L.Z.; Zia-Amirhosseini, P., "Basic Principles of Pharmacokinetics", *Toxicologic Pathology*, 23 (1995) 115-123.

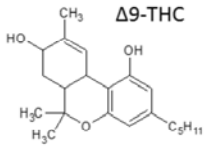
What makes a good drug candidate:

RO5 – Rule of Five – Lipinski's Rule of Five

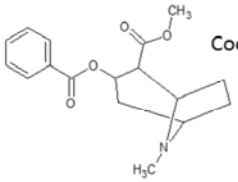
1. No more than 5 H-bond donors
2. No more than 10 H-bond acceptors
3. <500 amu molecular mass
4. Octanol:H_2O partition coefficient < 5

Modified Rules:

1. Octanol:H_2O partition coefficient -.04 < P < +5.6
2. Molar Refractivity from 40 to 130
3. Polar Surface Area < 140 $Å^2$
4. 10 or fewer Rotatable Bonds



Δ9-THC



Cocaine

JWH-018