

Data collated and provided courtesy by Ruth Perkins, B.S., M.S., Pharm.D.

Metabolites of opiates

DRUG	METABOLITES	Active for analgesia?	Active for side effects?	Accumulates in renal failure	Accumulates in hepatic failure	Liver enzyme	References
Morphine	M3G	No	Yes	Yes	No		Milne 1996
	M6G	Yes	Yes	Yes	No		Milne 1996
	normorphine						Milne 1996
Codeine	morphine	Yes	Yes	No	Yes	2D6	Mohammed 1993, Poulsen 1996
	M3G	No	Yes	Yes	No		Mohammed 1993, Poulsen 1996
	M6G	Yes	Yes	Yes	No		Mohammed 1993, Poulsen 1996
	inactive metabolites						Mohammed 1993, Poulsen 1996
Hydromorphone	H3G	?		Yes			Hagen 1995
	dihydromorphone	not in humans					Hagen 1995
	dihydroisomorphine	“ “					Hagen 1995
Oxycodone	noroxycodone			Yes			Kirvela 1996
	oxymorphone			Yes?			Kirvela 1996
Oxymorphone	look in merck index						
Buprenorphine	norbuprenorphine						Kuhlman 1996
Butorphanol	hydroxybutorphanol			Yes			Vachharajani 1997, Vachharajani 1996
	norbutorphanol						
Meperidine	normeperidine	No	Yes	Yes			Hardman, 1996
Fentanyl		No	No	No		3A4	Hardman 1996
Sufentanil	o-demethylated	Yes				3A4	Hardman 1996
Alfentanil						3A4	Hardman 1996
Methodone	pyrrolidines	No	No	No			Methodone and fentanyl are free of active metabolites and the elimination of the metabolites is independent of renal function, but there are no studies to say if they are neurotoxic
Propoxyphen	Data collated and provided courtesy by Ruth Perkins, B.S., M.S., Pharm.D.						
Hydrocodone							

Disease states affecting the pharmacokinetics of opiates

DRUG	Disease State	Pharmacokinetic parameter affected	Comments	References
Morphine	Acute Trauma	↓ Vd, ↓ Cl	Could be due to ↑ AAG and ↓ hepatic blood flow or enzyme activity.	Christie 1995
	Kidney failure	↑ AUC (M, M3G, M6G), ↓ Cl	Morphine should be used with caution due to accumulation of active metabolites.	Berkovitch 1994
Codeine	Sickle Cell	↓ t _{1/2}	Decrease probably due to a change in Vd, not clearance.	Mohammed 1993
Oxycodone	Renal transplant	↑ Vc, Vdss, t _{1/2} , ↓ Cl	Reduced Cl possibly due to alterations in hepatic blood flow and enzyme activity caused by uremia; excretion of metabolites may be severely impaired.	Kirvela 1996
Butorphanol	Elderly	no significant changes	No significant differences were found when using transnasal butorphanol to dictate a dosage change.	
	Hepatic impairment	↑ AUC, t _{1/2} , Vdss, F ↓ Cl	The authors suggested to leave the initial dose unchanged, but subsequent dosing intervals should be prolonged. The % of reduction in Cl was highly correlated to the degree of portosystemic shunts.	Vachharajani 1996
Meperidine	Renal failure		Accumulation of metabolite occurs.	Reisine 1996
	Elderly			Erstad 1997
Fentanyl	Renal transplant	↑ t _{1/2} ↓ Cl	Data was compared with previously published literature values. The authors suggested that a BUN > 60 mg/dl is associated with a low fentanyl clearance.	Koehntop 1997
Sufentanil	Head trauma	No significant changes	The authors commented that sufentanil itself exerts no increase in intracranial pressure.	Scholz 1994
	Liver transplantation, cirrhosis	t _{1/2} =11.28 +/- 3.4 hrs	Significant extrahepatic clearance occurs during the anhepatic phase – may be preferred over alfentanil which has not demonstrated extrahepatic clearance	Raucoules-aime 1997, Ferner 1985, Chauvin 1989
Alfentanil	ICU patients	↑ t _{1/2} , Vdss	The authors stated that the ↑ Vd and ↓ Cl compensate for each other leading to a good correlation between predicted and actual serum concentrations. They did not notice any considerable accumulation during long term infusions (24h).	Frenkel 1995
	Chron's disease	No significant changes	The authors stated that the increased alfentanil requirements in Chron's patients may be due to pharmacodynamics not pharmacokinetics.	Gesink-Van Der Veer 1993
Methadone				
Propoxyphene				
Hydrocodone				

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