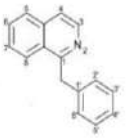
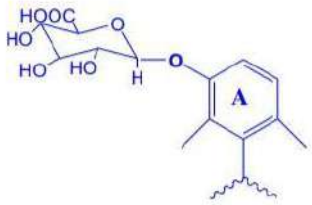
Apomorphine

Morphine: Stereochemistry

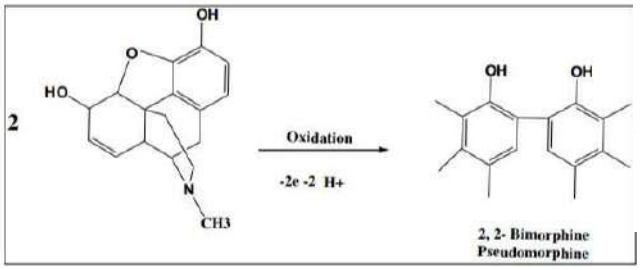


BENZYLISOQUINOLINE
Papaverine 0.8-1%
Noscapine 3-10%
Narcine 0.2-0.4%

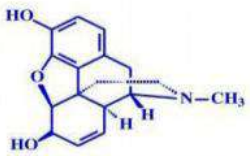
OPIUM PHENANTHRENE
Morphine 9-14%
Codeine 0.5-2%
Thebaine 0.2-1%



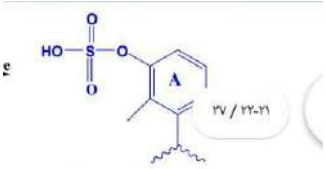
Morphine -3-O- glucuronide
No analgesic activity



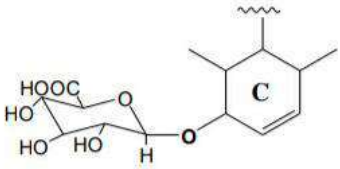
2, 2- Bimorphine
Pseudomorphine



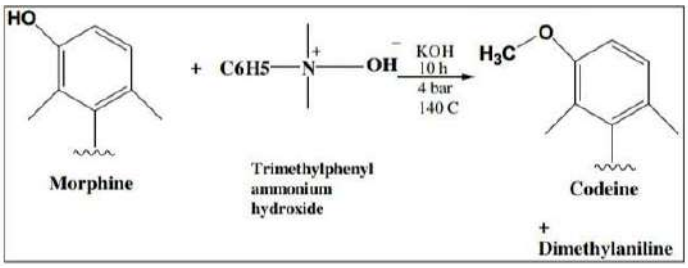
"Unnatural" Morphine (the mirror image)
No analgesic activity



3-O-Sulfate conjugate
Note 6-O-sulfate conj is active



Morphine -6-O-glucuronide
Analgesic activity



Morphine

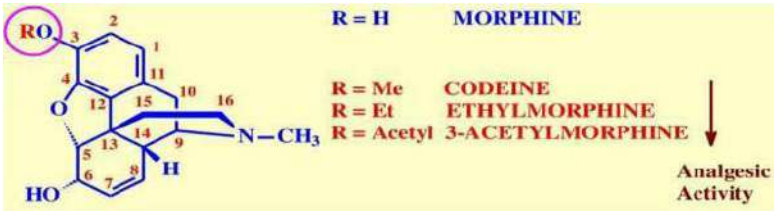
Trimethylphenyl ammonium hydroxide

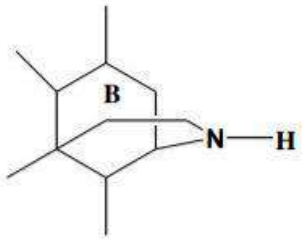
Codeine

+ Dimethylaniline

Alcoholic and phenolic OH : Heroin

R: CH3 CO-
R: CH3CO-

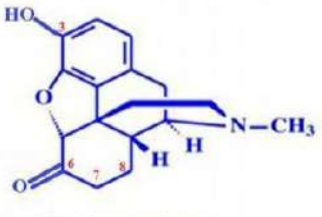




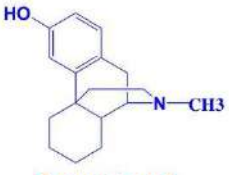
Normorphine

Oxycodone

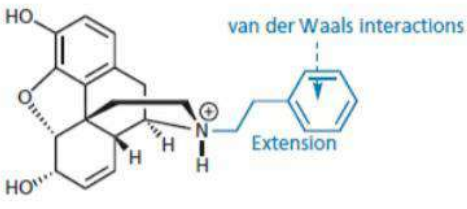
Hydrocodone



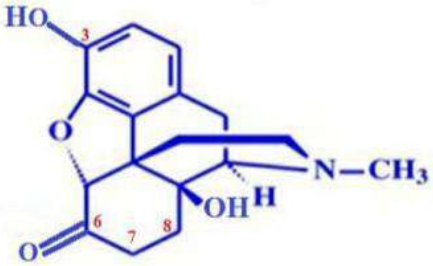
Hydromorphone



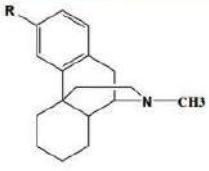
Levorphanol



N-Phenethylmorphine
(14 × activity of morphine)

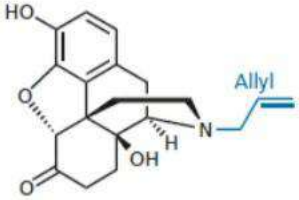


Oxymorphone

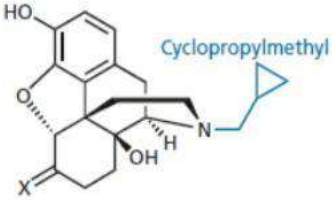


R: OH Levorphanol
R: OCH3 Dextromethorphan

Morphinan derivatives



Naloxone



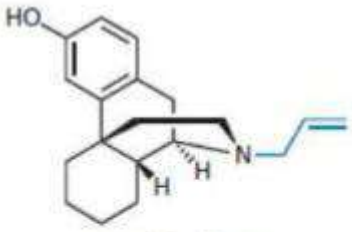
Naltrexone (X = O)
Nalmefine (X = CH_2)

Oxymorphone

Log D at pH7.4 : 0.32

Hydromorphone

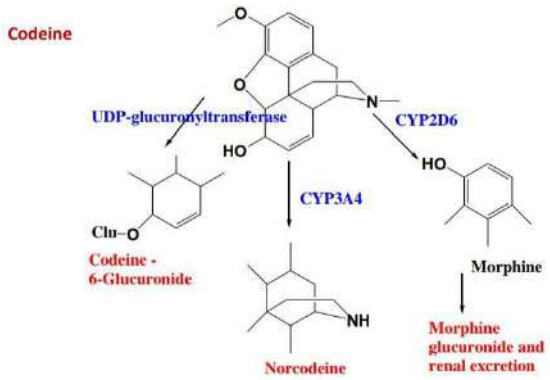
Log D at pH7.4 : 1.56



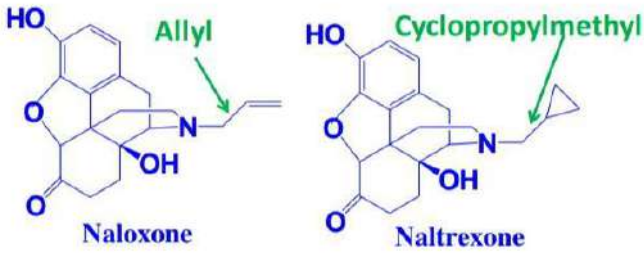
Levallorphan
(Antagonist 5 × more potent than nalorphine)

Nalorphine

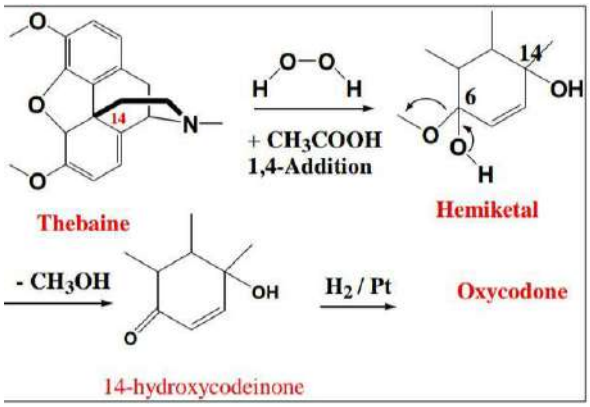
Nalorphine is **antagonist at μ-receptor**
Analgesic effect **agonist κ- receptor**

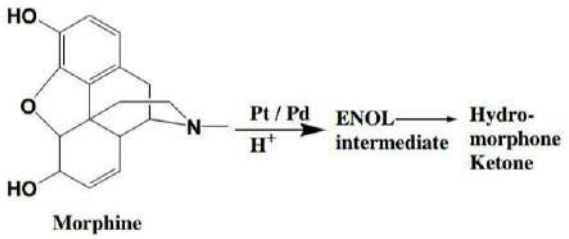


Remember



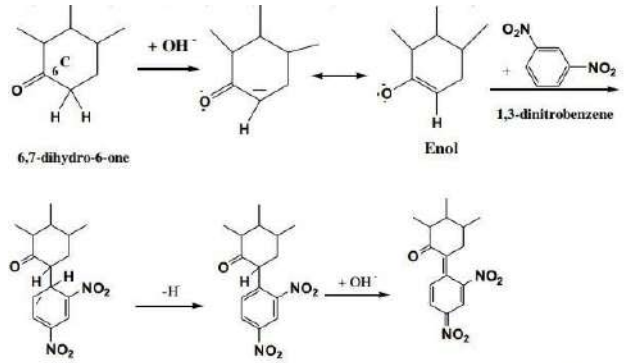
Pure antagonist



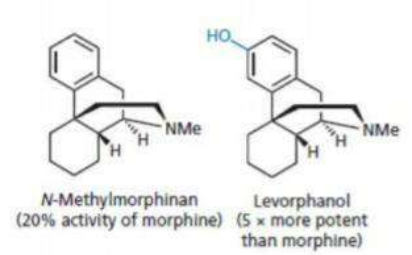


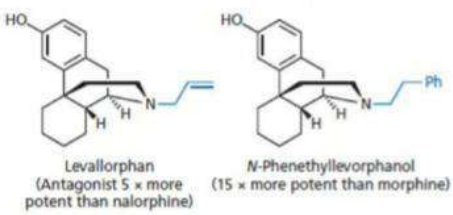
(+) Dextromethorphan

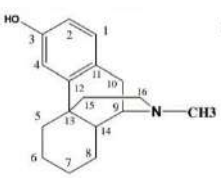
Antitussive



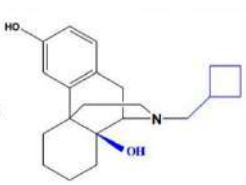
Zimmerman product
colored compound



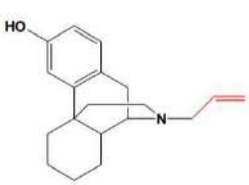




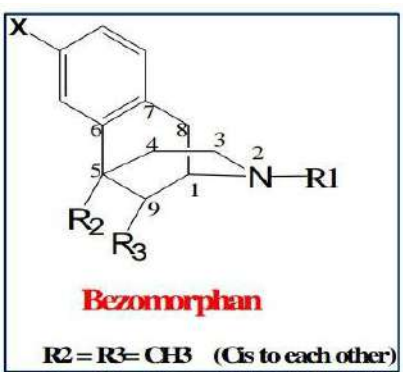
Levorphanol
Agonist, levo-isomer



Butorphanol
Mixed agonist antagonist

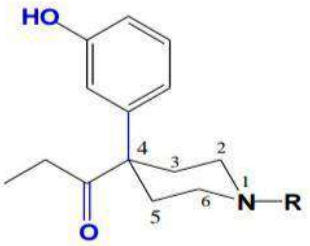


Levallorphan
Antagonist

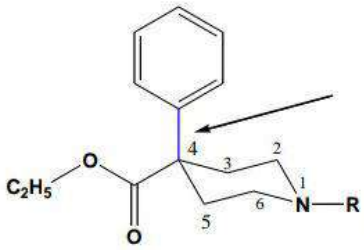


Bezomorphan

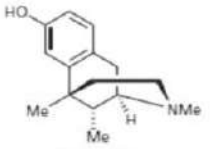
R2 = R3= CH3 (Cis to each other)



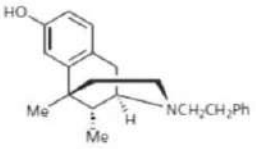
R: CH3 Ketobemidone



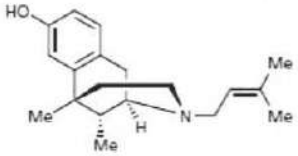
R: CH3 Meperidine



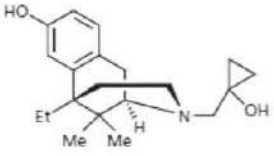
Metazocine
(same potency as morphine)



Phenazocine
(4 × more potent than morphine)

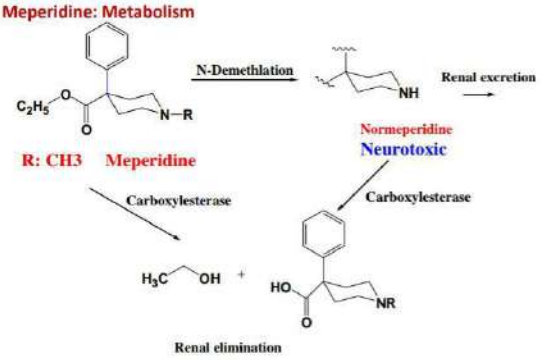


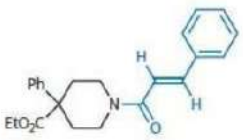
Pentazocine
(33% activity of morphine, short duration, low addiction liability)



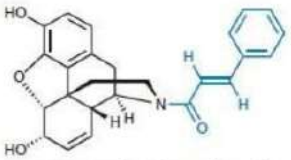
Bremazocine

Meperidine: Metabolism

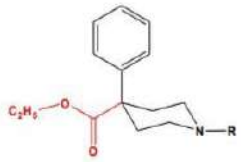




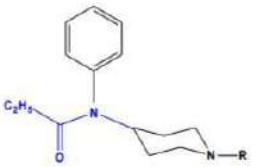
N-Cinnamoyl analogue of pethidine
30 × more potent than pethidine



N-Cinnamoyl analogue of morphine
Zero activity

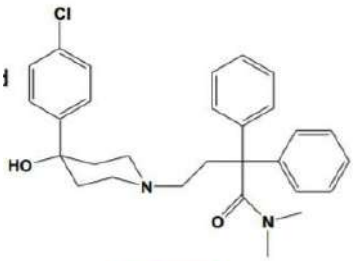


R: CH3 Meperidine

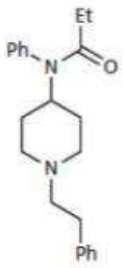


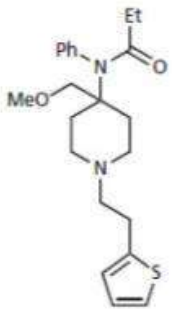
R: -CH2CH2Ph Fentanyl

100 X activity of morphine

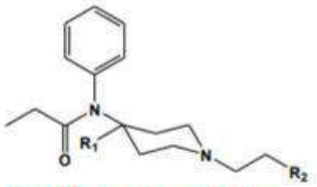


Loperamide





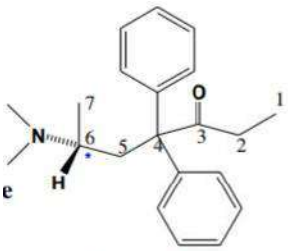
Fentanyl Sufentanil (Sufenta)



4-Anilidopiperidine derivatives

	R 1	R 2
Fentanyl	H	
Sufentanil	—CH2OCH3	

	R 1	R 2
Alfentanil	—CH2OCH3	
Remifentanil	—CO_2CH_3	—CO_2CH_3



levomethadone
Absolute configuration R
Levorotatory

Remifentanil

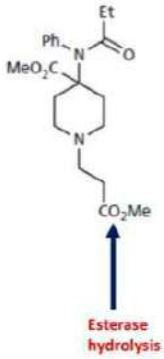
Short acting analgesic

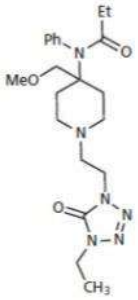
Ester group instead of aromatic ethyl substituent at piperidine

Ester is metabolized by esterases in the blood and tissue to a weakly active metabolite (1:300–1:1,000 the potency of remifentanil

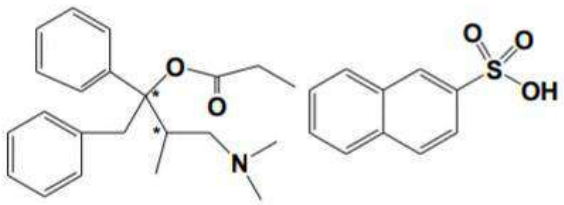
Rapid distribution across BBB (1 minute).
High Log P, pKa: 7.07

The ester hydrolysis leads to a quick recovery (5–10 minutes)

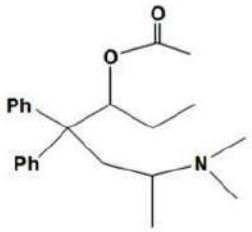




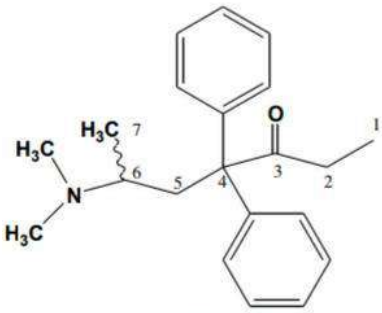
Alfentanil (Alfenta)



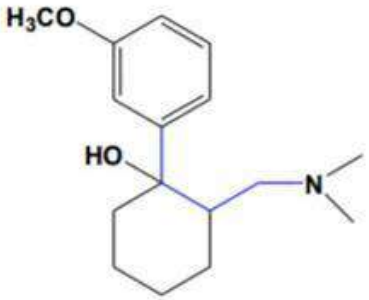
Propoxyphene napsylate



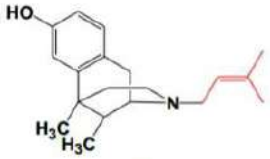
L-alpha-Acetylmethadol [LAAM]
more potent than methadone
long duration (one dose every 3 days)



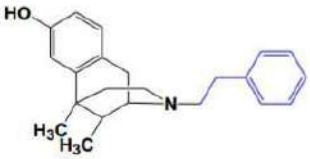
Methadone



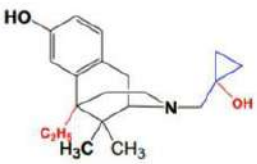
Tramadol



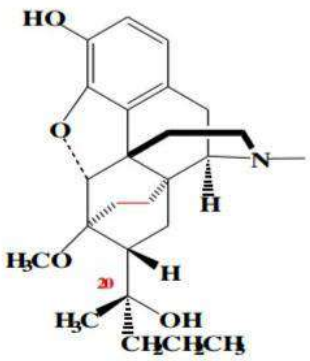
Pentazocine
Mixed agonist antagonist



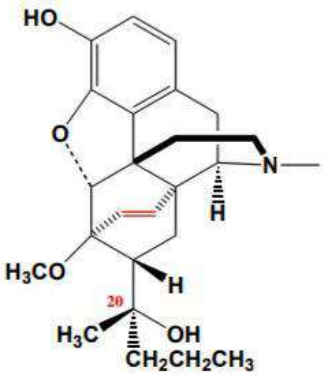
Phenazocine
Agonist 4X morphine



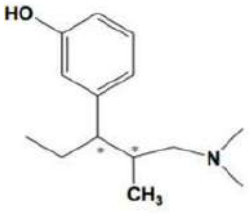
Bremazocine
200X morphine



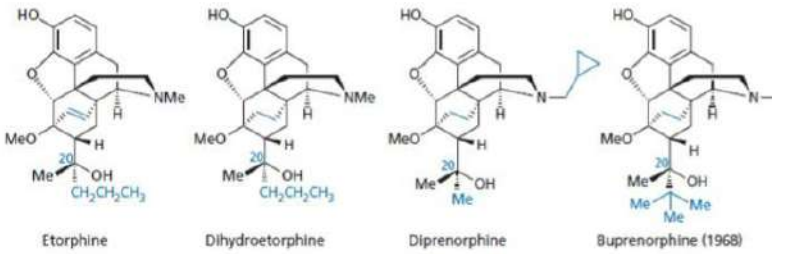
Dihydroetorphine



Etorphine

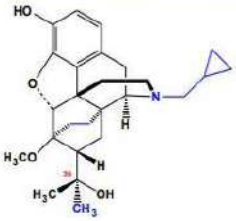


Tapentadol

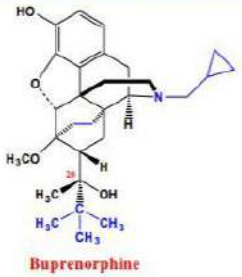


Etorphine | Dihydroetorphine | Diprenorphine | Buprenorphine (1968)

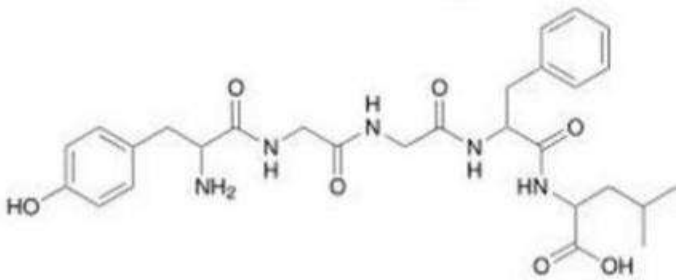
FIGURE 24.21 Etorphine and related structures.



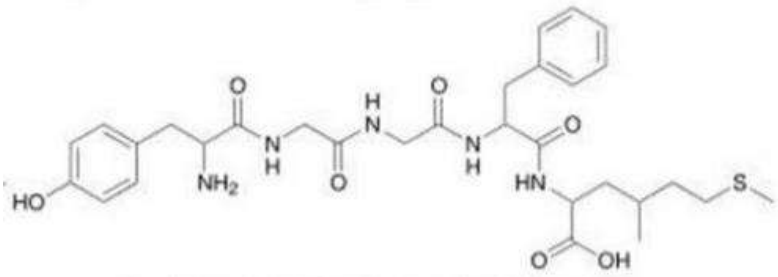
Diprenorphine



Buprenorphine



H_2N-Tyr-Gly-Gly-Phe-Leu-COOH
Leu-enkephalin



H_2N-Tyr-Gly-Gly-Phe-Met-COOH
Met-enkephalin