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# Opioids, or The Little Flower That Could



Image courtesy of [Louise Joly](#)

# So what's an opioid?

- **natural opiates**, alkaloids contained in the resin of the opium poppy including morphine, codeine, thebaine, papaverine, and noscapine
- **semi-synthetic opiates**, created from the natural opioids, such as hydromorphone, hydrocodone, oxycodone, and heroin
- **fully synthetic opioids**, such as fentanyl, pethidine, methadone, and propoxyphene
- **endogenous opioid peptides**, produced naturally in the body, such as endorphins, enkephalins, dynorphins, and endomorphins. Endorphins are regularly released in the brain and nerves, attenuating pain. Their other functions are still obscure, but may be related to opioid effects besides analgesia (antitussin, anti-diarrheal).

# Okay, that's great, but what do they *do*?

- Opioids are agonists to four endogenous neurotransmitters.
  - $\beta$ -endorphin
  - leu-enkephalin
  - Dynorphin
  - Met-enkephalin
- Opioid receptors are found primarily in the CNS and GI tract. The body responds to exogenous opioids in the brain by reducing (and sometimes stopping) production of the endogenous opioids.

# Tell me more about these opioid receptors.

- G-protein coupled receptors: the  **$\mu$ -opioid receptor**.
- ~40% identical to somatostatin receptors (SSTRs).
- Some functions:
  - analgesia, sedation, euphoria
- Some adverse effects of drugs that act on them:
  - nausea, vomiting, drowsiness, constipation, respiratory depression
- The  $\mu$ -binding sites are discretely distributed in the human brain, with high densities in the posterior amygdala, hypothalamus, thalamus, nucleus caudatus, putamen, and certain cortical areas. They are also found on the terminal axons of primary afferents within laminae I and II (substantia gelatinosa) of the spinal cord and in the spinal nucleus of the trigeminal nerve.

# Neato. So why do folks use opioids?

- Clinically, used in palliative care for pain.
  - Recently, often used to manage chronic pain, which is now considered safe if used with care and alongside drugs which deal with other elements of pain (NSAIDS) and the opioid side effects (antihistamines, stimulants).
  - Examples of modern opioids include **morphine**, **fentanyl**, **oxycodone**, and **tramadol**.
- Illegally, for recreational drug use.
- Historically, for analgesia, insomnia, depression/anxiety (medicinal); and for euphoria, pleasure (recreational).

# Hold on a sec. Historically? How old ARE these things?

Well, people have been using the opium poppy to relieve pain and to make themselves happy since the Neolithic, and the ancient world – Sumeria, Minoa, Assyria, Egypt, Greece, Rome, Persia, Arabia – definitely made use of opium.

There are a few historically important forms:  
**Opium**, **Laudanum**, **Morphine**, and **Heroin**.

# Opium

- Narcotic made from the sap of immature seed pods of the opium poppy
- Contains up to 15% morphine, as well as codeine, papaverine, and noscapine
- Used medicinally since ancient times, recreational use began in China in the 15th century and spread, significantly under the auspices of the British Empire



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# Laudanum

- Alcoholic tincture of opium. Created 16th century by Paracelsus, famous chemist. Such a good analgesic he called it Laudanum, from the latin laudare, to praise.
- 19th century, used in many patent medicines. One of the more efficacious drugs of the time, by Victorian era it was widely used and abused. Given for all sorts of complaints, even to infants. (And mad wives, poets, fretful women...)



[Image courtesy of the National Institutes of Health.](#)

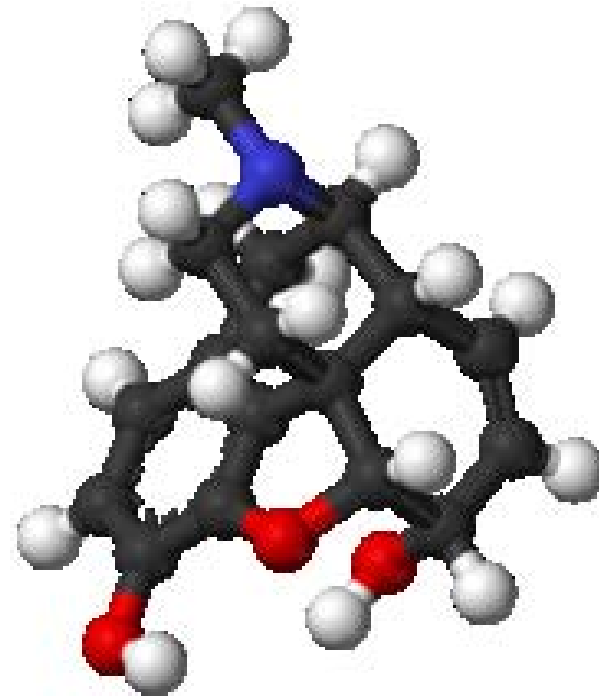
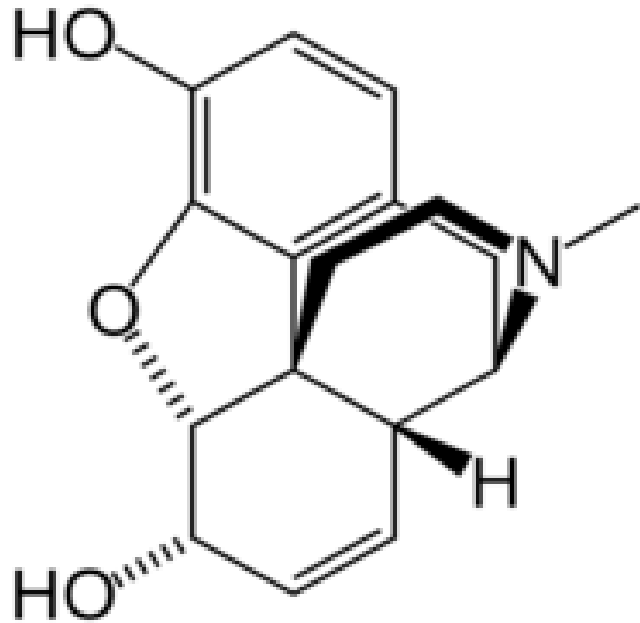
# Morphine

- Analgesic and sedative.  
Name is from Morpheus, god of sleep.
- Drug is derived from opium, but the chemical also exists as a natural endocrine product in some animals, including humans
- Extremely potent, highly addictive, with tolerance and both physical and psychological resistances developing quickly
- Prototype narcotic drug and is the standard against which all other opioids are tested
- It interacts predominantly with the  **$\mu$ -opioid receptor.**



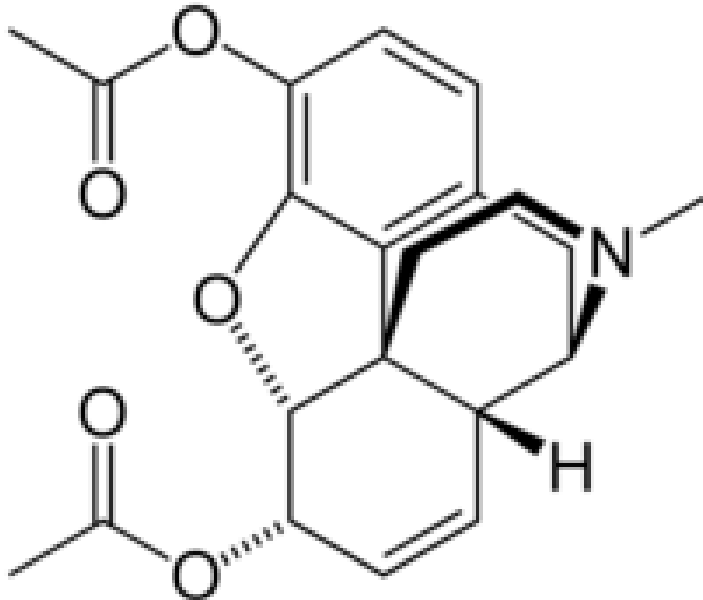
Image courtesy of [Zerpheus](#).

# And for the chemists...



# Heroin

- Diacetylmorphine: 3, 6-diacetyl ester of morphine. The acetyl groups allow the drug to quickly cross the blood-brain barrier by rendering it more lipid-soluble than morphine.



- Binds to  $\mu$ -opioid receptors resulting in intense euphoria with the feeling centered in the gut.
- Highly addictive, fairly nasty withdrawal symptoms, and is now illegal. Schedule 1 controlled substance, which means you probably ought to stay away from it, eh?

# Wait, “is now illegal”?

Correct, heroin was first created as a drug, and seen as not only fairly harmless, but indeed quite useful. How about a quick trip down a chemist's memory lane? Well, two of them, to be precise:  
C.R. Alder Wright and Felix Hoffman.

# C.R. Alder Wright

- First person to create heroin
- An English chemist who had been researching the effects of combining morphine with various acids
- Made heroin by boiling anhydrous morphine alkaloid with acetic anhydride
  - The resultant chemical was seen to produce *interesting* effects in young dogs and rats, but was mostly ignored.

# Felix Hoffman

- Felix Hoffman of Bayer later re-discovered heroin while looking for a way to produce codeine from morphine
  - Hoffman named his drug from how subjects felt after taking it - 'heroisch', or heroic.
- Heroin was first marketed by Bayer as non-addictive morphine substitute. It was sold as a cough medicine for children and prescribed as a treatment for morphine addiction.
  - Something of a modern corporate embarrassment, really.



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So opioids have a lot of history, widespread use, and great potential for help and harm.

- **The Good:**

- **Relief from Pain**
- **Relief from Depression**
- **Feeling Happy, Euphoric**

- **The Bad:**

- **Tolerance**
- **Dependence**
- **Addiction**
- **Possibility of Death**