

# **Narcotic Analgesics**

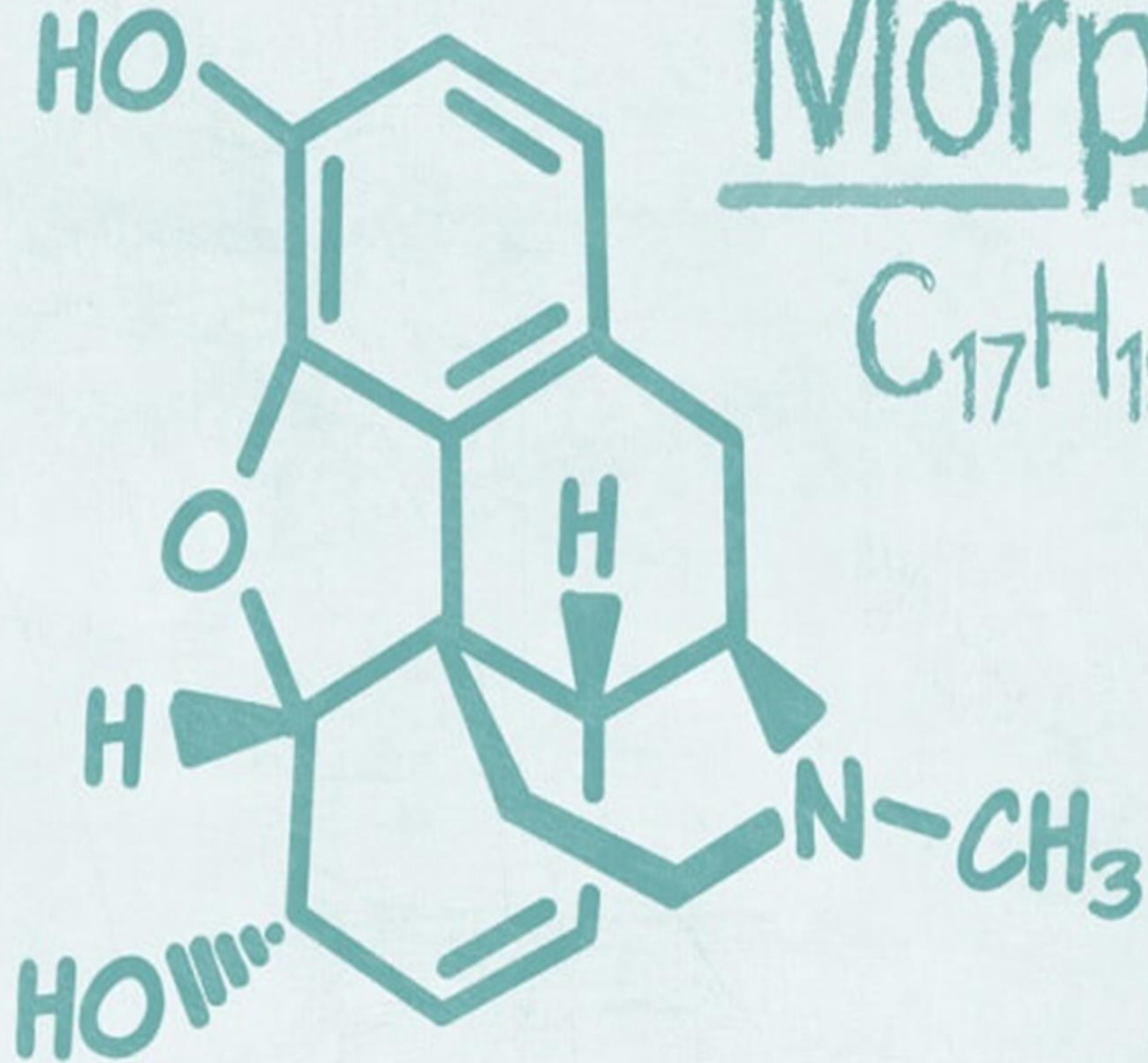
By

L.A Shahad Al-Imarah

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# Morphine



## Phenanthrenes Opioid Receptors

## Action

*Morphine*

Agonist

*Codeine*

Agonist

*Oxycodone*

Agonist

*Oxymorphone*

Agonist

*Hydromorphone*

Agonist

*Hydrocodone*

Agonist

*Buprenorphine*

Partial agonist

*Nalbuphine*

Mixed Agonist/Antagonist

*Butorphanol*

Mixed Agonist/Antagonist

*Pentazocine*

Mixed Agonist/Antagonist

# MOA

- ▶ Analgesic drugs found in crude- opium includes : **Morphine** ;is the prototype strong  $\mu$  receptor agonist while **Codeine**; is less potent & the weak prototype of opioid agonists.
- ▶ Interacting stereo-specifically with opioid receptors

on the membranes of certain cells in the CNS, the gastrointestinal (GI) tract and the urinary bladder.

**Morphine** *also* decreases substance P produced by **K Receptors** in dorsal horn of the spinal cord, Substance P modulates pain perception.

# Actions

- ▶ Analgesia
- ▶ **Euphoria**
- ▶ Respiration
- ▶ Depression of cough reflex
- ▶ Miosis
- ▶ Emesis
- ▶ GI tract
- ▶ Cardiovascular
- ▶ Histamine release
- ▶ Hormonal Actions
- ▶ Labor

# Analgesia

Opioids like *Morphine* have analgesic effect (pain relief without the loss of consciousness)

A. raising the pain threshold at the spinal cord level

B. altering the brain's perception of pain.

Patients on opioids are still aware of the presence of pain, but the sensation is not unpleasant.

*Morphine* is the prototype opioid agonist.

Opioids are used for pain in trauma, cancer, and other types of severe pain.

# Euphoria

- ▶ *Morphine* produces a powerful sense of contentment and well-being.
- ▶ Euphoria may be caused by disinhibition of the dopamine-containing neurons of the ventral tegmental area.

# Respiratory Depression

- ▶ Opioids reduce the sensitivity of respiratory center neurons to **CO<sub>2</sub>**.
- ▶ Tolerance to this effect does develop quickly with repeated dosing, which allows the safe use of *morphine* for the treatment of pain when the dose is correctly titrated.
- ▶ **Emesis** Morphine stimulates the chemoreceptor trigger zone in the area postrema that causes vomiting.



- ▶ **Depression of cough reflex**: Morphine does suppress cough reflex, but **codeine** and **dextromethorphan** are more commonly used.
- ▶ **Miosis**: The pinpoint pupil (**Figure 14.8**) characteristic of morphine use results from stimulation of  $\mu$  and  $\kappa$  receptors. There is little tolerance to the effect, and all morphine abusers demonstrate pinpoint pupils.



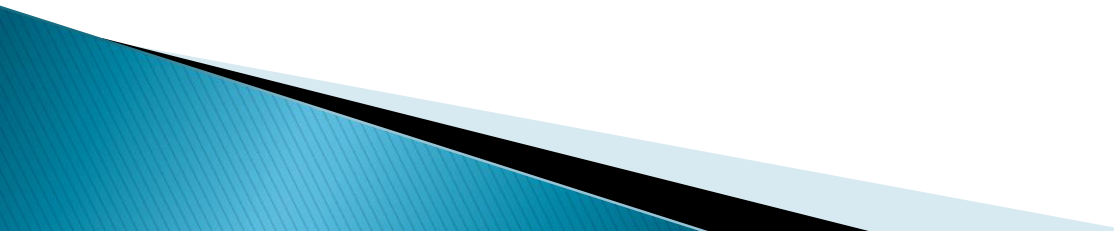
- ▶ Opioids decrease GI motility and increase the tone of intestinal circular smooth muscle.

Most common opioid **Anti-diarrheal** are:

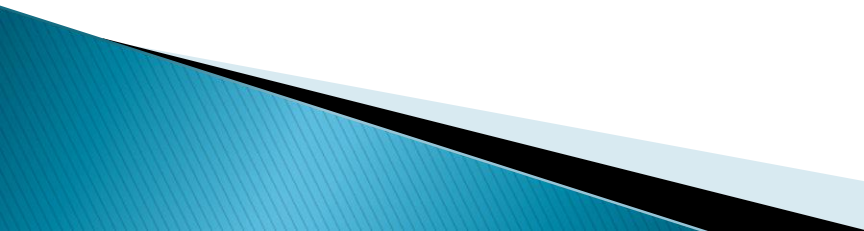
**Diphenoxylate** and **Loperamide**

**Anaesthesia (?)**: Opioids are used as preanesthetic medications (not anaesthetic by themselves), for systemic and spinal anesthesia for postoperative analgesia.

# Morphine ADMET

- ▶ Its significant 1<sup>st</sup> pass metabolism of **Morphine** most often given intramuscular & subcutaneous.
  - ▶ Oral **Morphine** is commonly formulated as an extended-release.
  - ▶ *Morphine* rapidly distribute to all tissues including placenta.
  - ▶ Infants of addicted mothers show physical dependence and exhibit withdrawal symptoms if no opioids are given.
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# Side Effects

- ▶ Severe **Respiratory Depression** is most dangerous SE, hence most cases of opioid overdose cause death.
  - ▶ **Tolerance and physical dependence**
  - ▶ **Drug interactions:** depressant actions of morphine are enhanced by phenothiazines, monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants.
  - ▶ Hence many OD when above drugs are taken by morphine addicts.
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# *Codeine*

naturally opioid less active than morphine.  
should be used only for mild to moderate pain.

Codeine is converted to Morphine by the **CYP450 2D6** enzyme system which varies between patients.

Ultra-rapid metabolisers may experience higher levels of morphine, leading to possible overdose.

**Codeine+ acetaminophen** is commonly used for pain management.



# *Codeine*

**Codeine** has very good antitussive activity at non-analgesic doses.

Codeine cough syrup must be medically prescribed.

In non-prescription cough syrup, codeine has been replaced

By:

**Dextromethorphan**; a synthetic cough depressant that has relatively no analgesic action and a relatively *low potential for abuse*.



# References

- ▶ Lippincott Chapter 14
  - ▶ Pages 191–204
- ▶ Figure 14.2, 14.3, 14.9, 14.12
  - ▶ Lecture Notes