Narcotic Analgesics : Opioids

Over view & definitions

Natural & Endogenous opioids system

Naturally occurring compounds have been identified as a family of polypeptides produced by the brain and pituitary gland , these involve :

- **β - Endorphin** (for "endogenously produced morphinelike compound").
- **Enkephalins**
- **Dynorphin**

The endogenous opioid system is inactive under normal conditions, but when activated by stressors it can block the transmission of pain.

Exogenous opioids such as opium and morphine can produce euphoria, and so endogenous opioids may mediate reward or positive reinforcement pathways.

Pain is defined as an unpleasant sensation that can be either acute or chronic and is a consequence of complex neurochemical processes in the peripheral and central nervous systems (CNS).

It is subjective, and the clinician must rely on the patient's perception and description of pain.

Analgesic : compounds or drugs reduce pain sensation , Management of pain is one of clinical medicine's greatest challenges.

Opiates: are drugs derived from opium a powdered, dried exudate of the fruit capsule (poppy) of the plant *Papaver somniferum* . these includes (**morphine, heroin**) .

Opioids: Opioids are drugs with morphine-like activity that produce analgesia (i.e., reduce pain) without the loss of consciousness and can induce tolerance and physical dependence.

Opioids are also referred to as **narcotic analgesics** , which are natural, semisynthetic, or synthetic compounds that produce morphine-like effects (Figure 14.2).

These agents are divided into chemical classes based on their chemical structure Clinically this is helpful in identifying opioids that have a greater chance of cross-sensitivity in a patient with an allergy to a particular opioid.

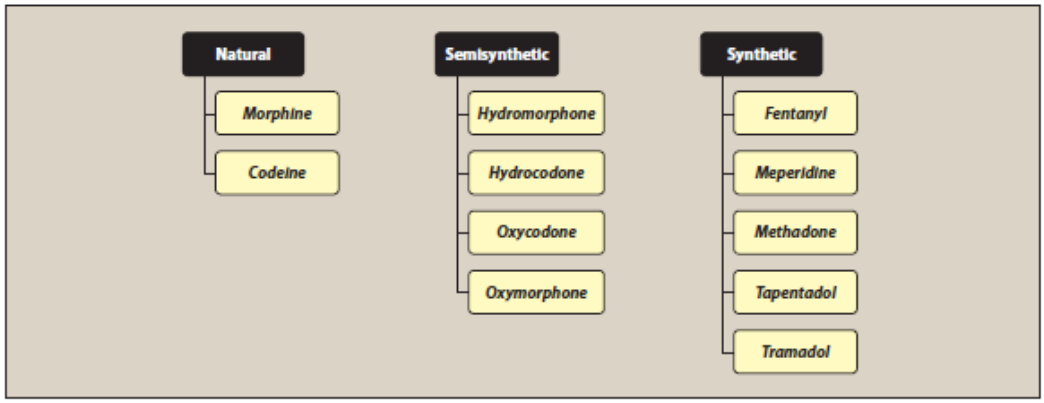

Figure 14.2
Summary of chemical classes of opioid agonists.

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Opioids Mechanism of action

All opioids act by binding to specific opioid receptors in the CNS to produce effects that mimic the action of endogenous peptide neurotransmitters (**endorphins, enkephalins) .**

Although the opioids have a broad range of effects, their primary use is to relieve intense pain, whether that pain results from surgery, injury, or chronic disease. Unfortunately, widespread availability of opioids has led to abuse of those agents with euphoric properties.

Antagonists that reverse the actions of opioids are also clinically important for use in cases of overdose .

OPIOID RECEPTORS

The major effects of the opioids are mediated by three receptor families, Each receptor family exhibits a different specificity for the drug(s) it binds these receptors are commonly designated as :

- ✓ **μ (mu) :** The analgesic properties of the opioids are primarily mediated by the μ receptors that **modulate responses to thermal, mechanical, and chemical nociception.**
- ✓ **κ (kappa) :** The κ receptors in the **dorsal horn** of the spinal cord also contribute to analgesia by modulating the response to **chemical and thermal nociception..**
- ✓ **δ (delta) :** The enkephalins interact more selectively with δ receptors in the periphery.

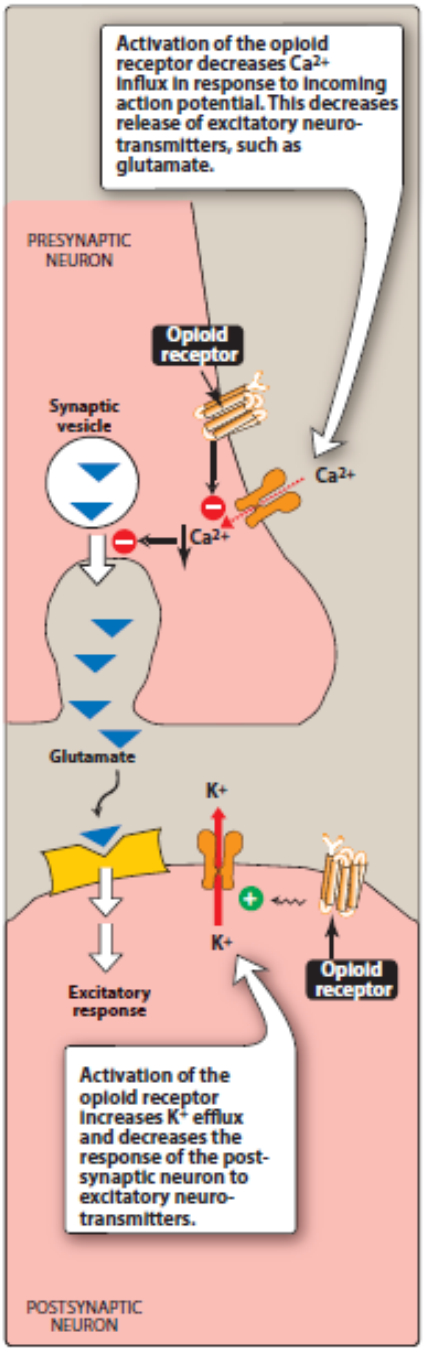
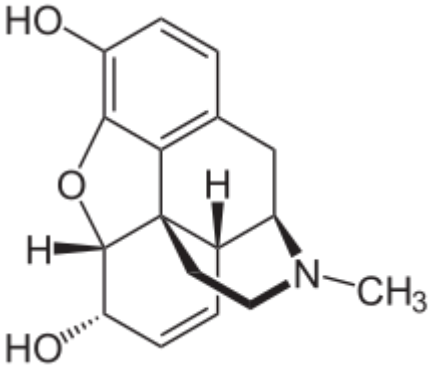


Figure 14.4
Mechanism of action of μ opioid receptor agonists in the spinal cord.

OPIOID AGONISTS

❖ Morphine

A-CLASS : Natural opioid alkaloid (opiates) derived as powdered exudate from opium fruit capsule (poppy) of the plant (opium) , act as opioid agonist



Therapeutic uses & Adverse effects

Some therapeutic uses of *morphine* and other opioids are

- **Analgesia:** *Morphine* and other opioids cause analgesia (relief of pain without the loss of consciousness) and relieve pain both by raising the pain threshold at the spinal cord level and, more importantly, by altering the brain's perception of pain.

Patients treated with opioids are still aware of the presence of pain, but the sensation is not unpleasant. The maximum analgesic efficacy for representative opioid agonists is shown in Figure 14.7.

- **Depression of cough reflex (Antitussive effect) :** Both morphine and codeine have **Antitussive** properties. In general, cough suppression does not correlate closely with the analgesic and respiratory depressant properties of opioid drugs.

The receptors involved in the antitussive action appear to be different from those involved in analgesia.

- **Anti-Emetic:** Morphine directly stimulates the chemoreceptor trigger zone (CTZ) in the brain that causes vomiting.

- **Anti-Diarreal action on GI tract:** Morphine relieves **diarrhea** by decreasing the motility and increasing the tone of the intestinal circular smooth muscle.

, produce constipation when used in combination with Antidiarrheal drugs .

Therapeutic Use	Comments
Analgesia	*Morphine* is the prototype opioid agonist. Opioids are used for pain in trauma, cancer, and other types of severe pain.
Treatment of diarrhea	Opioids decrease the motility and increase the tone of intestinal circular smooth muscle. [Note: Agents commonly used include *diphenoxylate* and *loperamide* (see Chapter 31).]
Relief of cough	*Morphine* does suppress the cough reflex, but *codeine* and *dextromethorphan* are more commonly used.
Treatment of acute pulmonary edema	Intravenous *morphine* dramatically relieves dyspnea caused by pulmonary edema associated with left ventricular failure, possibly via the vasodilatory effect. This, in effect, decreases cardiac preload and afterload, as well as anxiety experienced by the patient.
Anesthesia	Opioids are used as preanesthetic medications, for systemic and spinal anesthesia, and for postoperative analgesia.

Figure 14.6
Selected clinical uses of opioids.

Adverse effects:

Euphoria

Respiration

Miosis

Hormonal actions

Cardiovascular: Morphine has no major effects on the blood pressure or heart rate at lower dosages. **With large doses, hypotension and bradycardia may occur.**

Tolerance and physical dependence:

Repeated use produces tolerance to the respiratory depressant, analgesic, euphoric, and sedative effects of morphine. However, tolerance usually does not develop to the pupil-constricting and constipating effects of the drug.

Physical and psychological dependence can occur with morphine and with some of the other agonists.

Withdrawal produces a series of autonomic, motor, and psychological responses that incapacitate the individual and cause serious symptoms، although it is rare that the effects cause death.

Drug interactions : Drug interactions with morphine are rare، although the depressant actions of morphine are enhanced by phenothiazines, monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants (Figure 14.10).

- **Codeine**

Adverse effects : كما شرحت سابقا مع المورفين

- **Oxycodone and Oxymorphone**
- **Fentanyl**
- **Methadone**

OPIODS WITH MIXED AGONIST–ANTAGONISTS

Mixed Agonist–Antagonists: Drugs that **stimulate one receptor but block another**

- **Pentazocine**
- **Tramadol**

Opioid Antagonist

Naloxone

Summary of opioids drugs

Phenanthrenes	Action on Opioid Receptors
Morphine	Agonist
Codeine	Agonist
Oxycodone	Agonist
Oxymorphone	Agonist
Hydromorphone	Agonist
Hydrocodone	Agonist
Buprenorphine	Partial agonist
Nalbuphine	Mixed Agonist/Antagonist
Butorphanol	Mixed Agonist/Antagonist
Benzmorphan	
Pentazocine	Mixed Agonist/Antagonist
Phenylpiperidines	
Fentanyl	Agonist
Alfentanil	Agonist
Sufentanil	Agonist
Meperidine	Agonist
Diphenylheptane	
Methadone	Agonist

Figure 14.3
Origin of opioids: natural, semisynthetic, or synthetic.

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