NARCOTIC ANTAGONISTS

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NARCOTIC ANTAGONISTS

Prevents or abolishes excessive respiratory depression caused by the administration of morphine or related compounds. They act by competing for the same analgesic receptor sites. They are structurally related to morphine with the exception of the group attached to nitrogen.

CLASSIFICATION

i. Pure antagonists (e.g. naloxone, naltrexone).

ii. Partial agonists of nalorphine type (e.g. Nalorphine, levallorphan, and cyclazocine).

iii. Partial agonists of morphine type (e.g. propiram, profadol).
# Morphine-Related Antagonists

<table>
<thead>
<tr>
<th>General Structure</th>
<th>Name</th>
<th>R</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>Other</th>
<th>Therapeutic Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Morphine Structure" /></td>
<td>Nalorphine</td>
<td>—CH₂—CH = CH₂</td>
<td>H</td>
<td>OH</td>
<td>OH</td>
<td>—</td>
<td>Narcotic antagonist</td>
</tr>
<tr>
<td></td>
<td>Levallorphan</td>
<td>—CH₂—CH = CH₂</td>
<td>H</td>
<td>OH</td>
<td>H</td>
<td>a*</td>
<td>Narcotic antagonist</td>
</tr>
<tr>
<td></td>
<td>Naloxone</td>
<td>—CH₂—CH = CH₂</td>
<td>OH</td>
<td>OH</td>
<td></td>
<td>b**</td>
<td>Narcotic antagonist</td>
</tr>
<tr>
<td></td>
<td>Naltrexone</td>
<td>—CH₂—</td>
<td>OH</td>
<td>OH</td>
<td></td>
<td>b</td>
<td>Narcotic antagonist</td>
</tr>
<tr>
<td></td>
<td>Nalbuphine</td>
<td>—CH₂—</td>
<td>OH</td>
<td>OH</td>
<td>OH</td>
<td>b</td>
<td>Narcotic analgesic</td>
</tr>
<tr>
<td></td>
<td>Butophanol</td>
<td>—CH₂—</td>
<td>OH</td>
<td>OH</td>
<td>H</td>
<td>a, b</td>
<td>Narcotic analgesic</td>
</tr>
</tbody>
</table>

*ₐ = No o-atom between C₄ and C₅.

*ₐ* = No ‘double bond’ between C₇ and C₈.
Nalorphine

Uses:
• Also known as *N*-allyl normorphine, is a mixed opioid agonist–antagonist with opioid antagonist and analgesic properties.
• It was used as an antidote to reverse opioid overdose and in a challenge test to determine opioid dependence.
• It acts at two opioid receptors — the μ-opioid receptor, and at the κ-opioid receptor.
• Drug has side effects such as dysphoria, anxiety, confusion and hallucinations and for this reason, is no longer used medically.
Levallorphan

17-prop-2-enyl-17-azatetracyclo heptadeca-2(7),3,5-trien-4-ol

Uses:
- Also known as **levallorphan tartrate**, is an opioid modulator of the morphinan family.
- Levallorphan was formerly widely used in general anesthesia, mainly to reverse the respiratory **depression** produced by opioid analgesics and barbiturates used for induction of surgical anesthesia.
Naloxone (Allyl noroxymorphone)

17-Allyl-4,5α-epoxy-3,14-dihydroxymorphinan-6-one

Uses:
- **Narcan** (naloxone) is an opioid antagonist used for the complete or partial reversal of opioid overdose, including respiratory depression.
- **Narcan** is also used for diagnosis of suspected or known acute opioid overdose and also for blood pressure support in septic shock.
- **Narcan** is available in generic form.
NALOXONE:

1. It is N-allyl analogue of oxymorphone.

2. It selectively antagonises respiratory depression produced by morphine and other opioids.

3. Because of inactivation in the liver, it is potent on parenteral administration than on oral administration.

4. It is a pure antagonist. So by itself, naloxone does not produce respiratory depressant, analgesic or euphoriant effects.

5. It does not produce withdrawal symptoms. But it decreases the withdrawal symptoms of morphine and heroin.

6. It is used as an antagonist in opioid poisoning.
Receptor Empty
No Agonist = No Analgesic Action

Opioid Agonist
Receptor Occupied
Agonist = Analgesic Action
Analgesic Effect = Pain Lost

Opioid Antagonist
Receptor Occupied
Antagonist = Replace the Agonist
Toxicity Neutralized by Antagonist

Opioid Agonist Displaced
Receptor Occupied
