Analgesics
Objectives

- Describe the definition and classification of analgesics.

- Explain the screening method for analgesics.
Definition:

- Analgesics are drugs that selectively inhibit the perception “sensation” of pain.
### Types of Pain:

<table>
<thead>
<tr>
<th>Superficial</th>
<th>Deep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation of skin and mucous membrane.</td>
<td>Stimulation of muscles, joints and tendons.</td>
</tr>
<tr>
<td>Fast response “withdraw of limb”.</td>
<td>Slow response “sweating, nausea and vomiting”.</td>
</tr>
</tbody>
</table>
Classification of analgesics:

- Analgesics
  - Peripheral
    - Causal
    - Non causal
  - Central
    - Narcotics
    - Non-narcotics (NSAIDs)
### Classification of analgesics:

<table>
<thead>
<tr>
<th><strong>1. Peripheral</strong></th>
<th><strong>A. Causal</strong></th>
<th><strong>B. Non-causal</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Causal</strong></td>
<td>Treat the cause.</td>
<td>Do not treat the cause.</td>
</tr>
<tr>
<td><strong>Examples:</strong></td>
<td><strong>Examples:</strong></td>
<td></td>
</tr>
<tr>
<td>3. <em>Colchicine</em> treats gout.</td>
<td>3. <em>Counter-irritant</em> (apply pain that counteract or mask the original one e.g. acupuncture).</td>
<td></td>
</tr>
</tbody>
</table>
## Classification of analgesics:

<table>
<thead>
<tr>
<th>2. Central</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Narcotic (Opioid)</strong></td>
<td><strong>B. Non-narcotic (NSAIDs)</strong></td>
</tr>
</tbody>
</table>
| • Drugs have morphine like action.  
• Natural as codeine  
• Semisynthetic as dihydrodiacetylmorphine “heroin”  
• Synthetic as pethidine  
• Endogenous opiates as endorphin & encephalin | • Aspirin  
• Paracetamol  
• Ibuprofen  
• Diclofenac  
• Piroxicam  
• Ketoprofen |
## Classification of analgesics:

<table>
<thead>
<tr>
<th></th>
<th>NSAIDs</th>
<th>Narcotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site of action</strong></td>
<td>Subcortical “thalamus”.</td>
<td>Cortex &amp; thalamus.</td>
</tr>
<tr>
<td><strong>Antagonist</strong></td>
<td>None.</td>
<td>Naloxone, nalorphine &amp; levallorphan.</td>
</tr>
<tr>
<td><strong>Potency</strong></td>
<td>Low analgesic potency.</td>
<td>High analgesic potency.</td>
</tr>
<tr>
<td><strong>Uses</strong></td>
<td>Use in dull pain used in headache, backache &amp; toothache.</td>
<td>Sever &amp; deep pain used in cancer, MI &amp; angina pain.</td>
</tr>
</tbody>
</table>
## Classification of analgesics:

<table>
<thead>
<tr>
<th></th>
<th>NSAIDs</th>
<th>Narcotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Side effects</strong></td>
<td>• Increase in bleeding tendency and ulcer</td>
<td>• Addiction</td>
</tr>
<tr>
<td><strong>MOA</strong></td>
<td>• They inhibit PG synthesis by inhibiting COX enzyme.</td>
<td>• They cause direct activation of opiates receptors ($\mu$-$\kappa$-$\delta$).</td>
</tr>
<tr>
<td></td>
<td>• Stimulate the release of endorphin, enkephalin.</td>
<td>• Stimulate the release of endorphin, enkephalin.</td>
</tr>
</tbody>
</table>
Screening methods for analgesics:

**Principle:**

Pain is induced in a suitable animal and the animal response to the painful stimuli is recorded before & after the drug administration.
Screening methods for analgesics:

A- Narcotics:

1- Thermal methods:

- Hot-plate method
- Tail flick method

\{ Heat is the painful stimuli \}

Heat is the painful stimuli
Screening methods for analgesics:

B- Non - Narcotics:

1- Electrical method:

By applying a certain voltage to the metallic rods in order to produce pain in the animal.

2- Chemical method:

By injecting some irritant substances such as acetic acid or parabenzoquinone e.g. Writhing method.
Hot plate Method:

Materials:
- Animal: Mouse
- Instruments: Hot-Plate Analgesiometer
- Painful stimuli: Heat 55°C.
- Drug used: Morphine 0.5% 25mg/kg
- Animal response: Licking of feet or trying to jump out of the beaker.
Hot plate Method:

Procedure:

- Calculate the dose according to the animal weight.
- Adjust the temperature of the hot plate at 55°C.
- Drop the mouse on the hot-plate, the animal will show signs of discomfort such as licking of feet or trying to jump out of the beaker.
Hot plate Method:

- The normal reaction time is determined (which is the time from dropping the animal inside the beaker until it licks its feet or jumps out of the beaker. Normally occur within 20 sec).

- Inject the dose of morphine IP, wait 5 min. Then, the reaction time determined again after 5, 10, 15 min.
**Hot plate Method:**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Normal reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 min</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
</tr>
<tr>
<td></td>
<td>15 min</td>
</tr>
<tr>
<td>25 mg/kg</td>
<td></td>
</tr>
<tr>
<td>50 mg/kg</td>
<td></td>
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</tbody>
</table>
Tail flick Method:

**Materials:**

- **Animal:** Mouse.
- **Instruments:** Tail- flick Analgesiometer.
- **Painful stimuli:** Heat 130 °C.
- **Drug used:** Morphine 0.5%, 25mg/kg.
- **Animal response:** Flicking of the tail.
Tail flick Method:

**Procedure:**

- Cover the animal body except the tail leave it exposed to a heat from beam of light at 130\(^\circ\)C.
- Flicking the tail should occur in less than or equal to 6 sec "cutoff point".
Tail flick Method:

**Procedure:**

- Calculate the required dose of morphine and injected the animal IP, wait 5 min then record the reaction time every 5, 10, 15 min.
- Calculate the % maximal possible effects (%MPE).

\[
\% \ MPE = \frac{\text{postdrug treatment} - \text{predisug treatment}/\text{cutoff point}}{6} - \text{predisug treatment} \times 100
\]
Writhing Method:

Principle:

The painful stimuli induced by IP injection of an irritant substance e.g. Acetic acid.

Definition of writhing:

Stretching of the body, withdrawing the lower limb, and the abdomen touch the ground.
Writhing Method:

**Materials:**

- **Animal:** Mouse.
- **Painful stimuli:** acetic acid 0.6% 1ml/100gm IP.
- **Drug used:** Na salicylate 2% 100mg/kg & 200mg/kg IP.
- **Animal response:** writhing.
Writhing Method:

Procedure:

Control mouse:

Inject the calculated dose of acetic acid IP, the mouse will response by writhing. Count the onset and number of writhing per 10 min.

Second mouse:

Inject Na salicylate 100mg/kg IP, wait for 5min. Then inject acetic acid and calculate the onset & number of writhing.
Writhing Method:

Procedure:

Third mouse:

Inject the Na salicylate 200mg/kg IP, wait for 5min. Then inject the dose of acetic acid then calculate the onset & the number of writhing.
### Writhing Method:

#### Results:

<table>
<thead>
<tr>
<th>Animal</th>
<th>Drug</th>
<th>Onset of writhing</th>
<th>No. of writhing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Acetic acid (1ml/100gm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated I</td>
<td>Na salicylate (100mg/kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated II</td>
<td>Na salicylate (200mg/kg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
N.B:

- Na salicylate delays the onset of writhing and decreases the No. of writhing, this explains the analgesic property of NSAIDs.
- The No. of writhing should be measured within 10 min after the onset time (first writhe).
References