College of Pharmacy

Department of Pharmacology

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Analgesics

Objectives

- Describe the definition and classification of analgesics.

- Explain the screening method for analgesics.

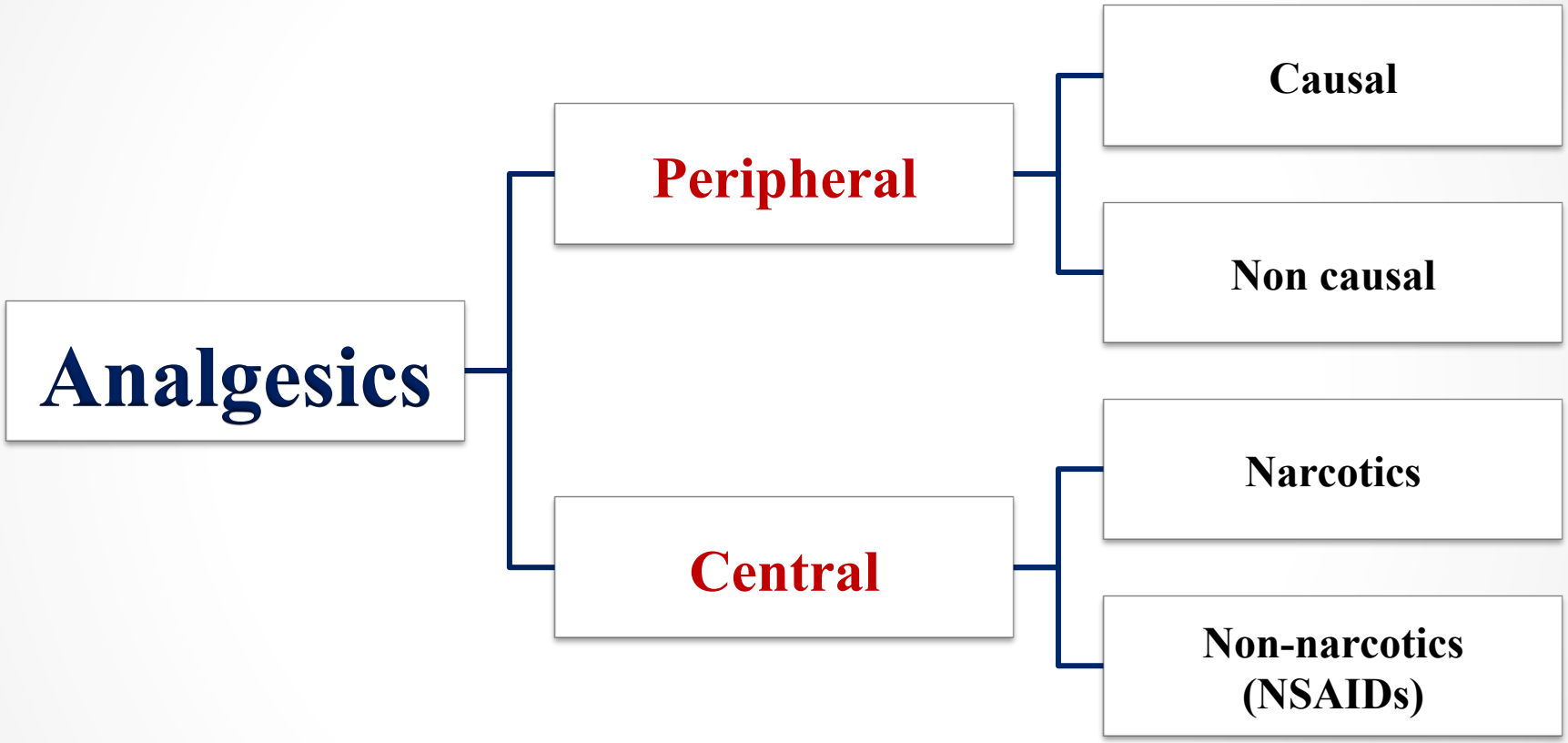
Definition:

- Analgesics are drugs that selectively inhibit the perception “sensation” of pain.

Types of Pain:

Superficial	Deep
Stimulation of skin and mucous membrane.	Stimulation of muscles, joints and tendons.
Fast response “withdraw of limb”.	Slow response “sweating, nausea and vomiting”.

Classification of analgesics:



Classification of analgesics:

1. Peripheral	
A.Causal	**B. Non-causal**
Treat the cause.	Do not treat the cause.
Examples: 1. **Atropine** relieves colic (antispasmodic). 2. **Ergotamine** treats migraine. 3. **Colchicine** treats gout.	**Examples:** 1. **Surface anesthesia** as eye. 2. **Local anesthetics** (for superficial tumor). 3. **Counter-irritant** (apply pain that counteract or mask the original one e.g. acupuncture).

Classification of analgesics:

2. Central	
A.Narcotic (Opioid)	**B. Non-narcotic (NSAIDs)**
•Drugs have morphine like action. •Natural as codeine •Semisynthetic as dihydro-diacetylmorphine "heroin" •Synthetic as pethidine •Endogenous opiates as endorphin & encephalin	•Aspirin •Paracetamol •Ibuprofen •Diclofenac •Piroxicam •Ketoprofen

Classification of analgesics:

	NSAIDs	Narcotics
Site of action	Subcortical “thalamus”.	Cortex & thalamus.
Antagonist	None.	Naloxone, nalorphine & levallorphan.
Potency	Low analgesic potency.	High analgesic potency.
Uses	Use in dull pain used in headache, backache & toothache.	Sever & deep pain used in cancer, MI & angina pain.

Classification of analgesics:

	NSAIDs	Narcotics
Side effects	•Increase in bleeding tendency and ulcer	•Addiction
MOA	• They inhibit PG synthesis by inhibiting COX enzyme.	• They cause direct activation of opiates receptors (μ-κ -δ). • Stimulate the release of endorphin, enkephalin.

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

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^{0}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^{0}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 .

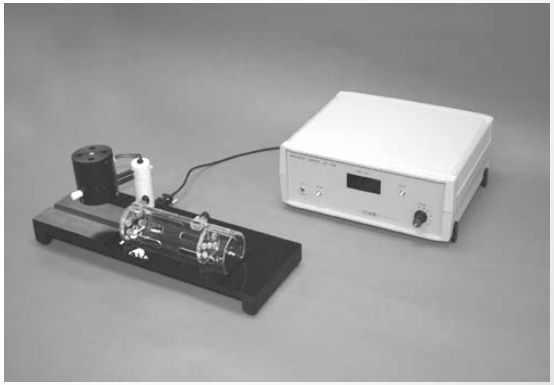
Hot plate Method:

Experiment	Normal reaction		
	5 min	10 min	15 min
25 mg/kg			
50 mg/kg			

Tail flick Method:

Materials:

- **Animal:** Mouse.
- **Instruments:** Tail- flick Analgesiometer.
- **Painful stimuli:** Heat 130 ºC .
- **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°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 5min then record the reaction time every 5, 10, 15min .
- Calculate the % maximal possible effects (%MPE) .

$$\%\ \boldsymbol{MPE = postdrug\ treatment - predrug\ treatment / cutoff\ point\ (6) - predrug\ treatment \times 100}$$

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.

Writing 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.

Writing 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.

Writing 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.

Writing Method:

Results:

Animal	Drug	Onset of writhing	No. of writhing
Control	Acetic acid (1ml/100gm)		
Treated I	Na salicylate (100mg/kg)		
Treated II	Na salicylate (200mg/kg)		

Writing Method:

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

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- Trevor, A. J. Katzung, B. G. and Masters, S. B. (2010). Local anesthetics. Basic and clinical pharmacology, 10th edition, Mc Graw Hill, San Francisco.