

Drug Therapy of Cough

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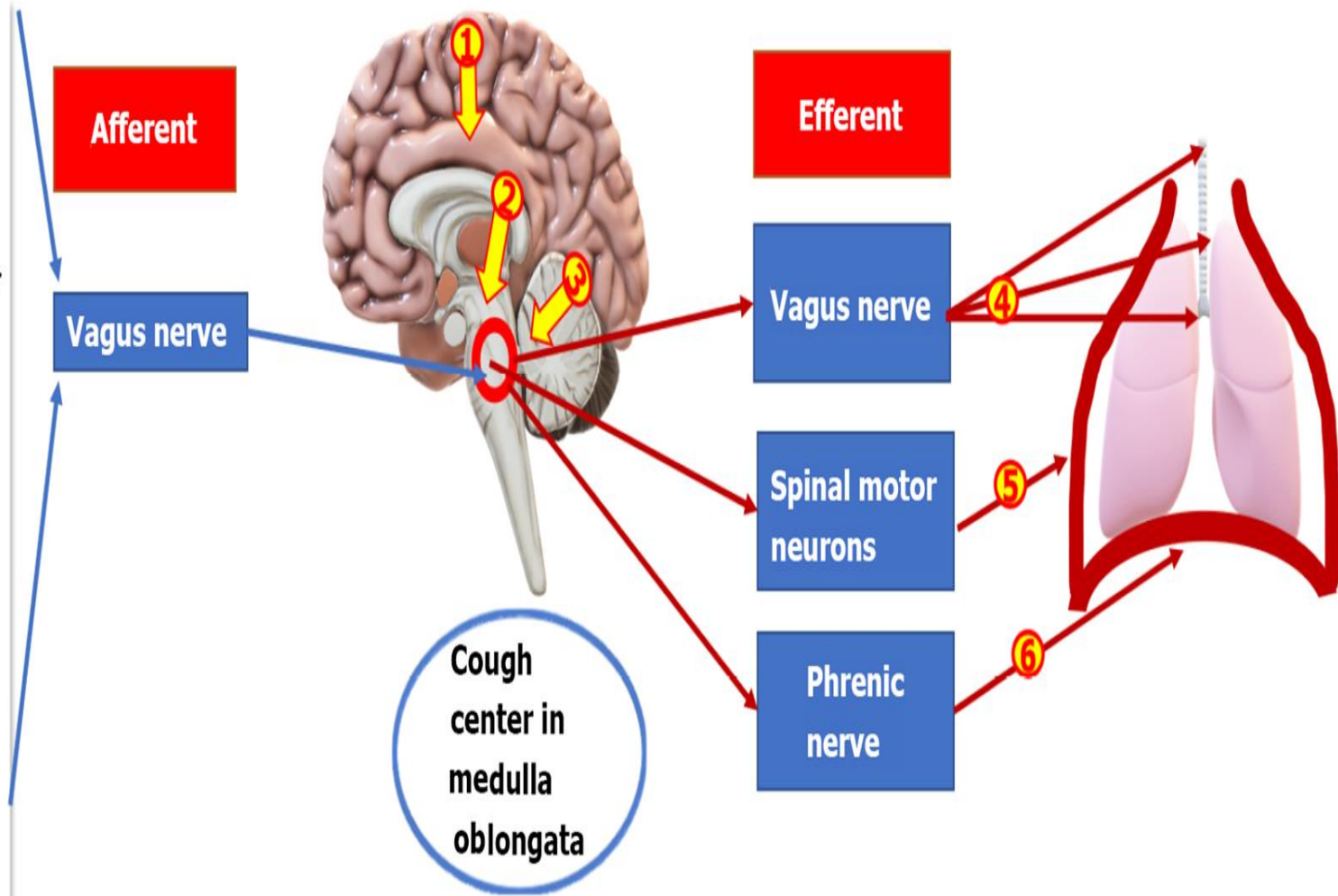


Receptors

Ear Drum and canal
Pharynx
Larynx and supralaryngeal area
Trachea (especially posterior wall and at the carina)
Bronchi
Terminal bronchioles and even the alveoli (chemical stimuli)
Esophagus
Pleura
Pericardium
Diaphragm
Stomach

Cough center with cortical and subcortical control

Action sites



- **Cough**

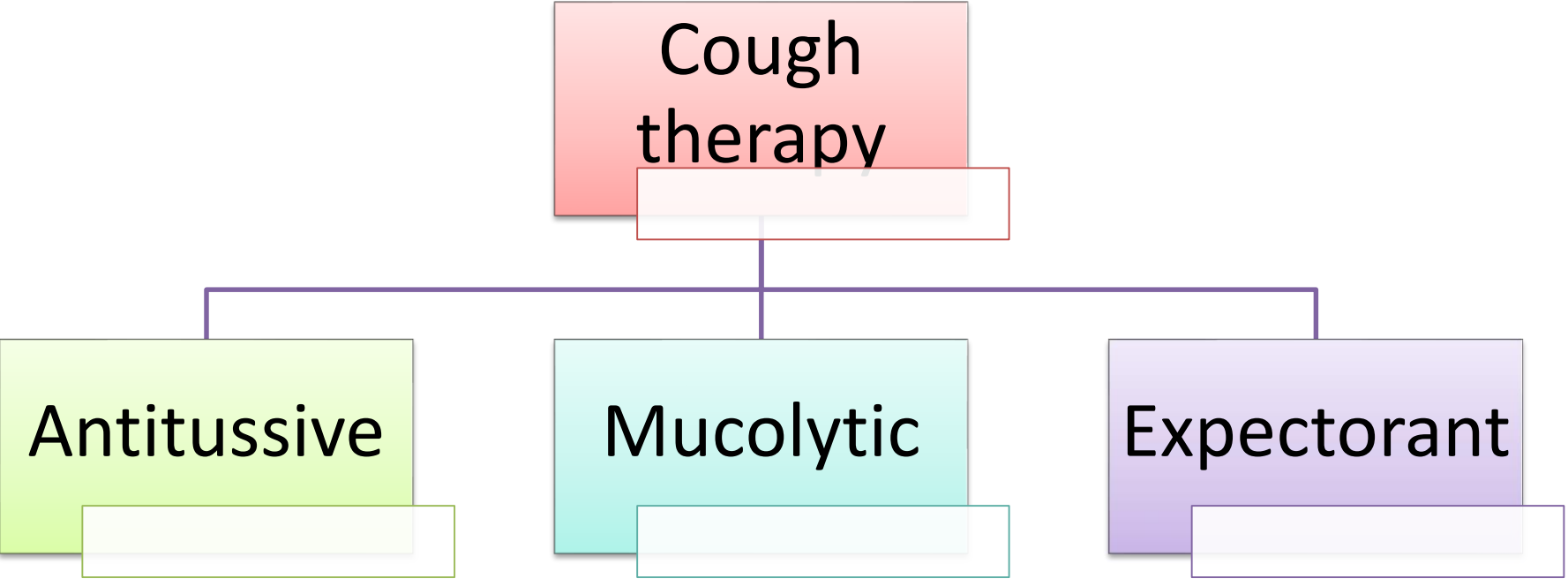
- is a protective reflex which serves the purpose of expelling sputum and other irritant material from the upper part of the respiratory airway.

- **There are two types of cough:**

productive cough (WET)

unproductive cough (DRY)

Cough
therapy



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graph TD; A[Cough therapy] --> B[Antitussive]; A --> C[Mucolytic]; A --> D[Expectorant];
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A hierarchical flowchart showing the classification of cough therapy. The root node is 'Cough therapy' in a red box. It branches into three categories: 'Antitussive' in a green box, 'Mucolytic' in a cyan box, and 'Expectorant' in a purple box. Each category box has a corresponding empty box below it, likely for a description or examples.

Antitussive

Mucolytic

Expectorant

ANTITUSSIVE

This is mediated through the use of antitussive drugs. They are classified into:

1. Central antitussives, that suppress the medullary cough center.
1. Peripheral antitussives, suppress the irritated sensory nerve endings which initiate the cough reflex.

1- Central antitussive

MOA: suppress cough by a direct action on the cough center.

CLASSIFIED: narcotic or a non-narcotic nature.

A-Narcotic antitussive

1-Mild addictive:

a-Codeine phosphate: orally given at night before sleep.

b- Dihydrocodeinone: orally

c-Pholcodine: This drug is mainly used as an antitussive.

It has little or no analgesic or euphoric action. Its addictive liability is claimed to be much less than that of codeine.

A/E: addiction liability, constipation, dysphoria, fatigue, and respiratory suppression.

2-High addictive drugs: morphine, methadone, and heroin

They are not commonly used as antitussives because of their addicting property.

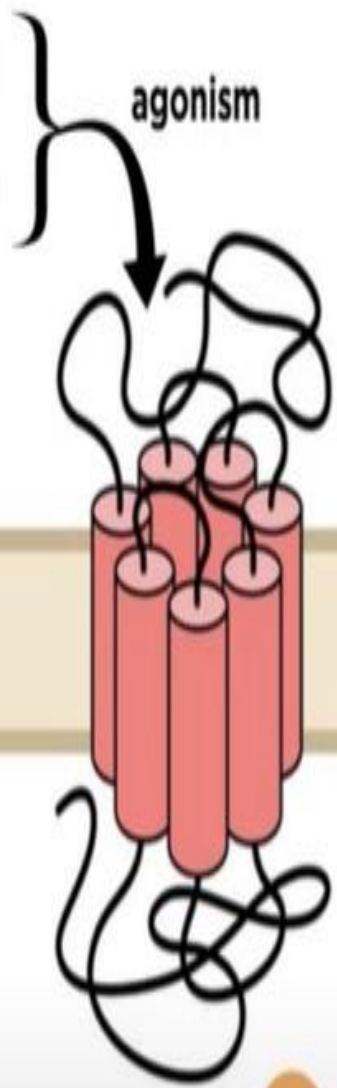
codeine-6-glucuronide



morphine



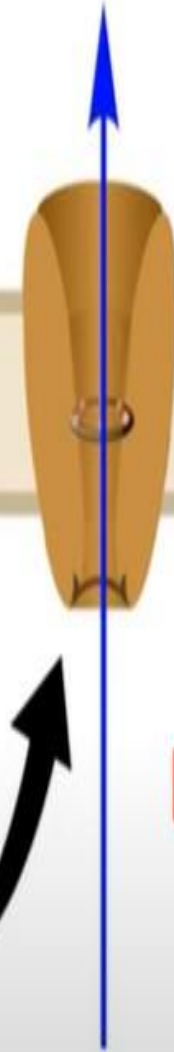
agonism



adenylate cyclase

Gai

inhibition



K⁺ channel

leads to hyperpolarization



Gβ

Gγ

B- Non-narcotic Antitussive

1- Opiate derivatives:

a-Dextromethorphan: this is a synthetic morphine substance has no analgesic or addictive properties. A/E: hallucinations and sedation.

b-Narcotine (noscapine): narcotine is a natural; opium benzylisoquinoline group with an antitussive action mainly.

Non-opiate derivatives:

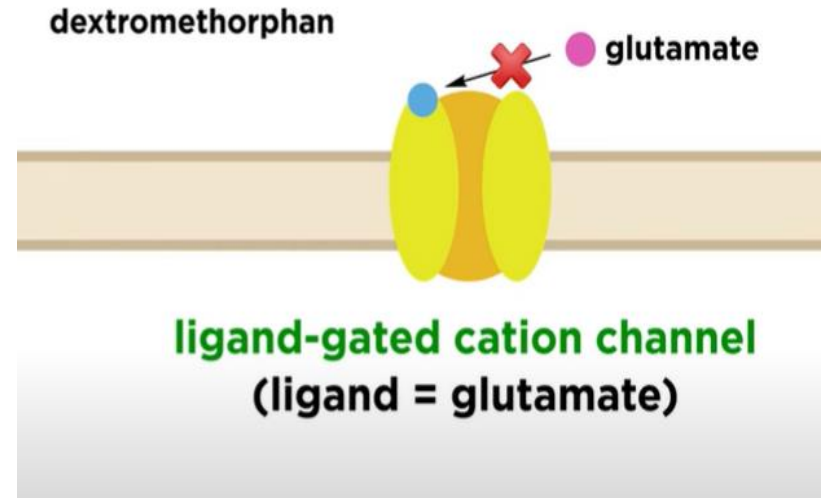
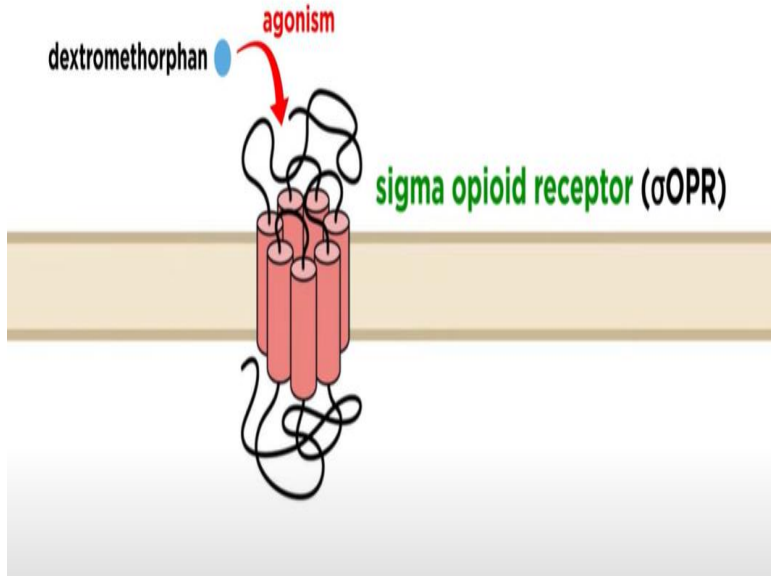
1-Benzonatate

2-Diphenhydramine (1st generation antihistaminic, anti-cholinergic)

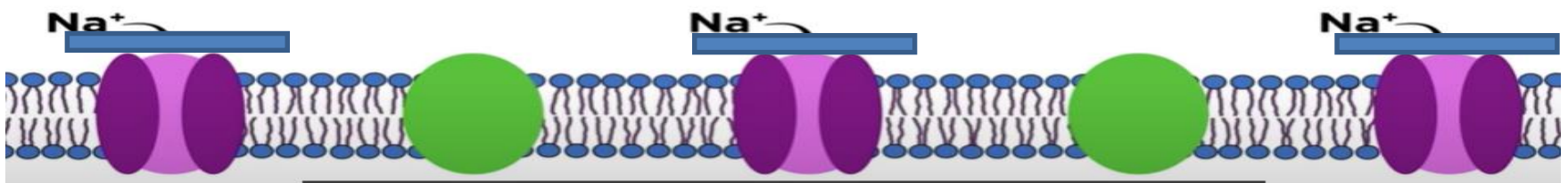
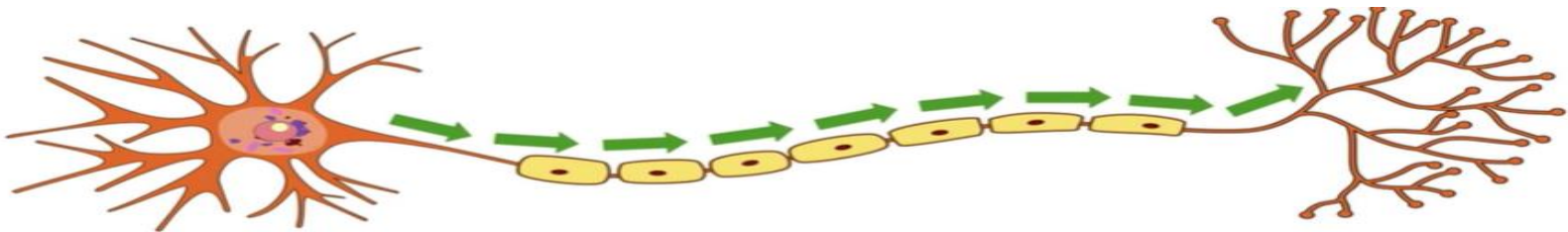
Dextromethorphan



MOA OF dextromethorphan



MOA OF benzonatate



B- Peripheral Antitussives

Drugs used in the treatment of mild to moderate cough. They inhibit cough receptors due to sore throat or laryngitis, (at the laryngeal level), or due to tracheitis and bronchitis (below laryngeal level).

Types:

1-Demulcents

2-Steam inhalation

3-Drugs with a local anesthetic activity

1-Demulcents

e.g: pastilles and lozenges. They often relieve coughs due to sore throat and pharyngitis, e.g. liquorice lozenges.



2-Steam inhalation

in tracheobronchitis, e.g. half a liter of boiling water to which is added a tea-spoonful of tincture benzoin or menthol promotes the secretion of protective mucus



3-Drugs with a local anesthetic activity

e.g. benzonatate, which reduces cough by depressing pulmonary stretch receptors. Benzonatate is chemically related to tetracaine. Benzonatate is given orally. It also has a central cough suppressant action.



Treatment of Productive Cough

- Treatment of useful cough is through the use of expectorant drugs.
- Expectorants facilitate the removal of respiratory tract secretion by coughing, thus, the paroxysms of coughing become less intense and less frequent.
- Expectorants may belong either to the sedative or to the stimulant type.

A. Sedative Expectorants

MOA: soothe the inflamed

respiratory mucosa by

stimulating the **secretion of**

protective mucus from the

secretory cells of the respiratory

airway. Thus, they increase the

fluidity of sputum and help its

expectoration by cough

They are classified into

1-Alkaline expectorants

2-Nauseant expectorants

3-Saline expectorants

B. Stimulant Expectorants (Aromatic Expectorants)

MOA: stimulates healing and repair, of the chronically inflamed respiratory mucosa, an action, described as a “vulnerary action”.

ACTIONS:

1-decrease the amount of sputum.

2-Deodorant action: the sputum loses its objectionable odor and taste.

3-Mild antiseptic action.

USES:

in the treatment of lung abscesses, chronic bronchitis, and bronchiectasis.

They include:

Creosote

Guaiacol

Terpene hydrate

1. Alkaline expectorants

e.g. sodium and potassium citrate and acetate.

- Citrate or acetates increase the alkali reserve of blood, the excess base being excreted through the bronchial glands, mildly stimulating them to secrete protective mucus.
- The drug further helps to dissolve mucus or sputum in the early stage of acute bronchitis.

2. Nauseant expectorants

- Nauseant expectorants stimulate sensory nerve endings in the stomach and set up a reflex resulting in a copious bronchial secretion.
- They may be used in the early dry stage of acute bronchitis.
- They are essentially emetics administered in subemetic doses



include:

- *Tincture ipecacuanha*, contains two irritant alkaloids, emetine and cephaline.
- *Tincture senega*
- *Ammonium chloride and carbonate*



3. Saline expectorants

sodium- and potassium **iodide**, given orally in the treatment of chronic bronchitis with tenacious sputum.

The iodides act by stimulating the bronchial secretory cells by direct action and liquifying the viscid sputum.

Contraindicated:

- 1-Acute bronchitis, as iodide ion may be too irritant for the bronchial mucosa.
- 2-Tuberculosis, as iodide ion might dissolve the fibrous tissue around an old tuberculous lesion, which may thus become reactivated.

Toxicity of iodide:

- 1- Sialadenitis (inflammation of salivary glands), rhinitis, gastritis, conjunctivitis,
- 2- Allergic manifestations.

MUCOLYTIC

Mucolytic are agents which help to liquefy viscid bronchial secretions without increase its amount. Consequently, they enhance the therapeutic efficacy of expectorants, but they are not true expectorants.

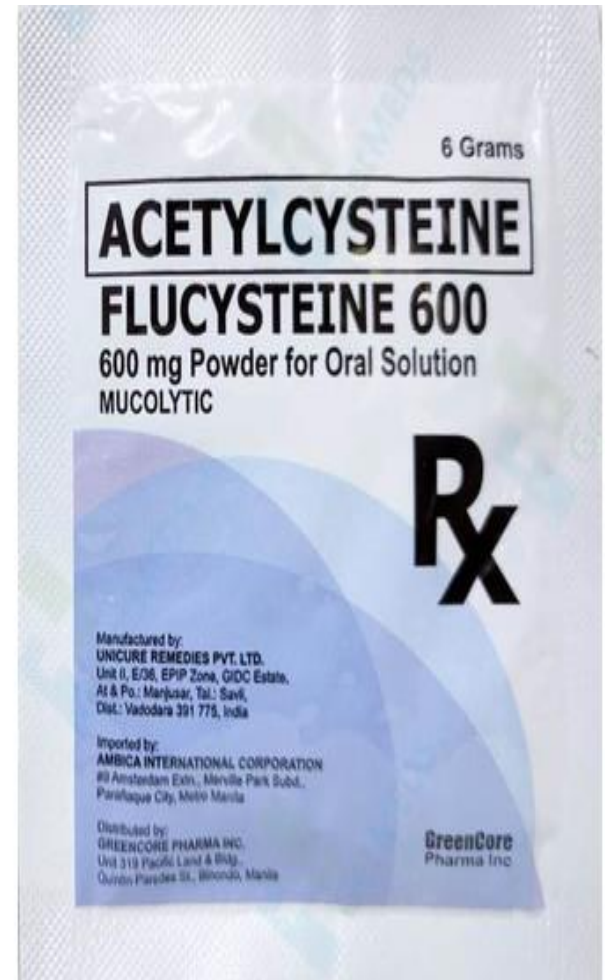
Bromhexine & Ambroxol

Acetylcysteine

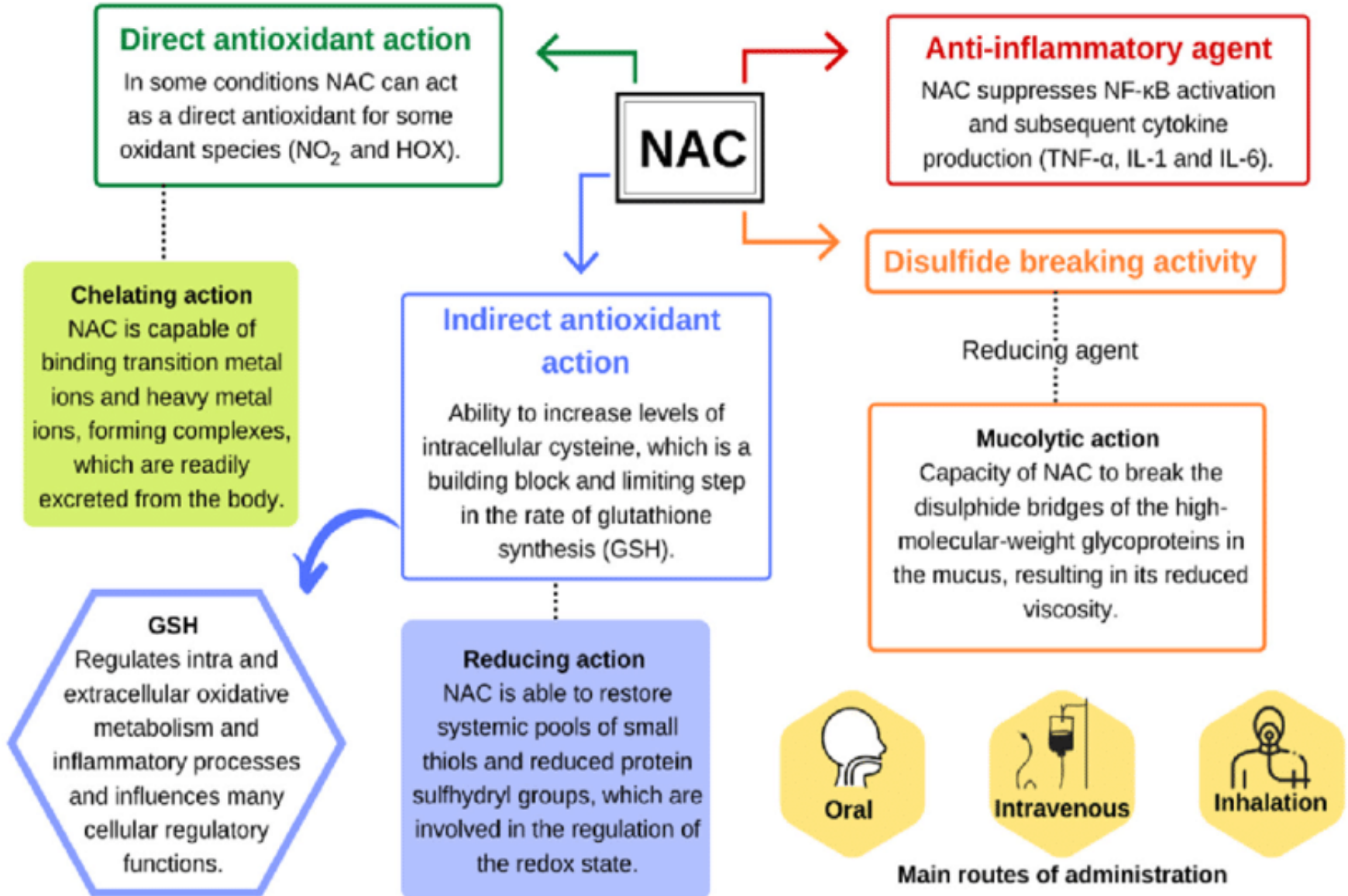
Carboxymethyl-cyteine

1- Acetylcysteine

- Acetylcysteine has a free sulphhydryl (SH) group that opens disulphide bonds in mucus-and reduces its viscosity.
- The drug is used as a 20% solution to liquefy viscous tracheobronchial **secretions.**
- It is administered by inhalation as an aerosol or is given by direct instillation into the tracheobronchial tree, through a tracheostomy or a bronchoscope.



Mechanisms of molecular action



2. Bromhexine & Ambroxol

Bromhexine reduces the viscosity of the bronchial secretion by depolymerization of the mucopolysaccharide, which forms the ground substance of the bronchial secretion.

3. Carboxymethyl-cysteine (mucodyne): (oral)

- In addition to its mucolytic property, the drug reduces the mucous gland hyperplasia which is usually associated with chronic bronchitis.
- It reduces sputum viscosity probably by its ability to split disulphide bonds linking strands of mucus.



Ambroxol

Expectorant

Release of surfactant and increase of bronchial secretions

Improvement of the rheological properties of the sputum

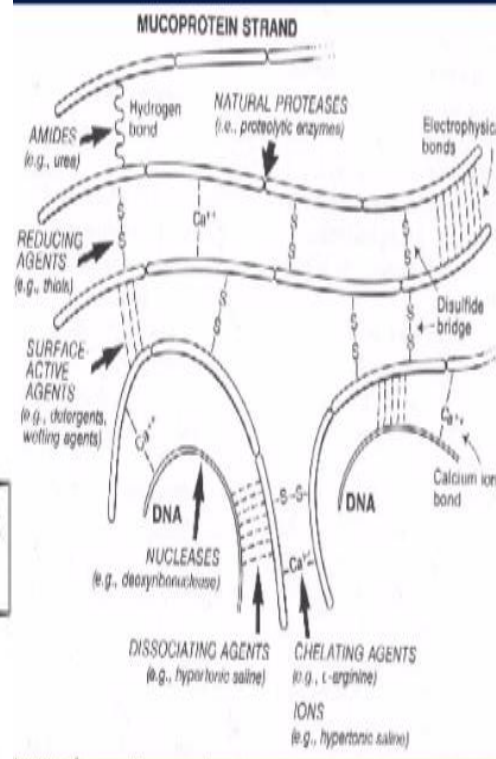
Increased mucus flow by cilia through coughing

Secretolytic

Depolymerisation of acidic polysaccharide fibers in the bronchial secretion

Thinner and less viscous sputum

Mucolytics: Bromhexine



- Causes Bronchorrhea
- It acts on the mucus at the formative stages in the glands, within the mucus-secreting cells.
- Bromhexine disrupts the structure of acid mucopolysaccharide fibres in mucoid sputum and produces less viscous mucus, which is easier to expectorate.

• **Expectorants** work by bringing moisture into the respiratory tract to help make mucus thinner.

• **Mucolytics** break down proteins and DNA in mucus so it's easier to cough it up.

• **Antitussive:** suppress coughing.

References

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Thank
you!!

