

DRUGS AFFECTING GIT MOTILITY

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Drugs affecting git motility

INCREASES

DECREASES

Prokinetics

laxatives

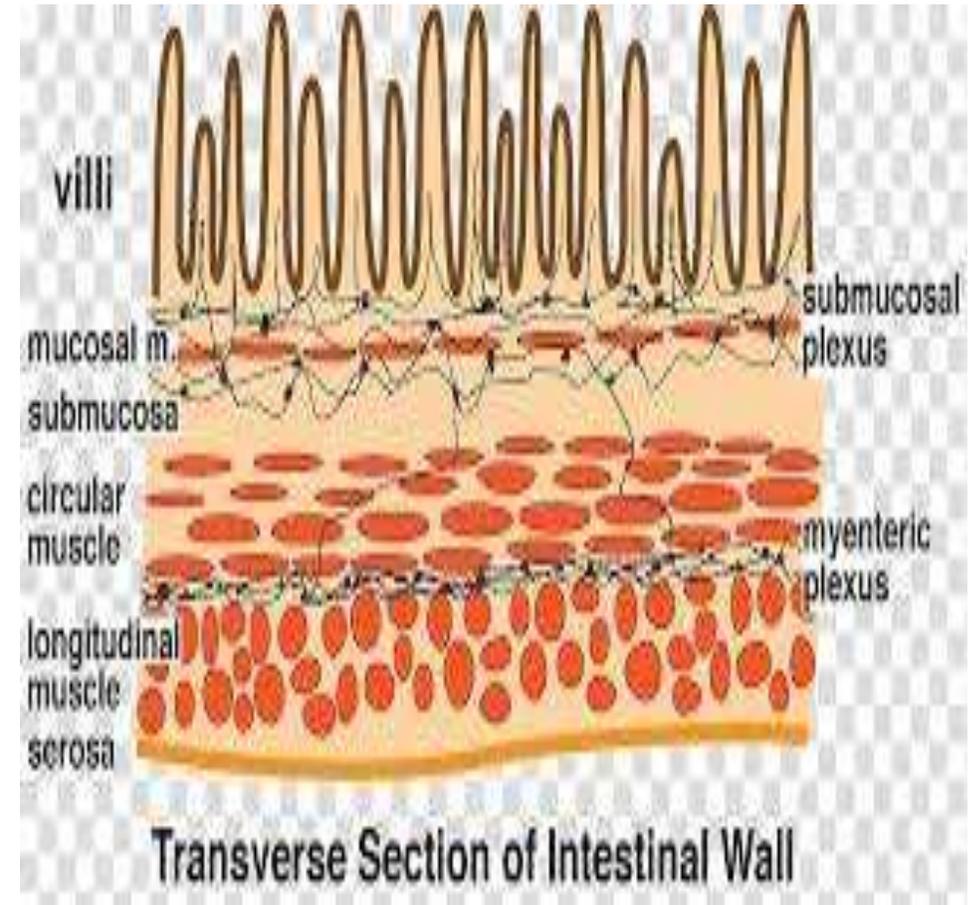
antispasmodic

antidiarrheal



Physiology of the Enteric Nervous System (ENS) (2nd brain):

- A network of ganglia cells & nerve fibers mainly located in gut wall.
- ENS can independently regulate G.I.T. motility & secretion.
- Although extrinsic sympathetic and parasympathetic nerves project onto the submucosal and myenteric plexuses, the (little brain outside CNS).



Main transmitters in ENS

SERETONIN(STIMULATORY +)

DOPAMINE(INHIBITORY -)

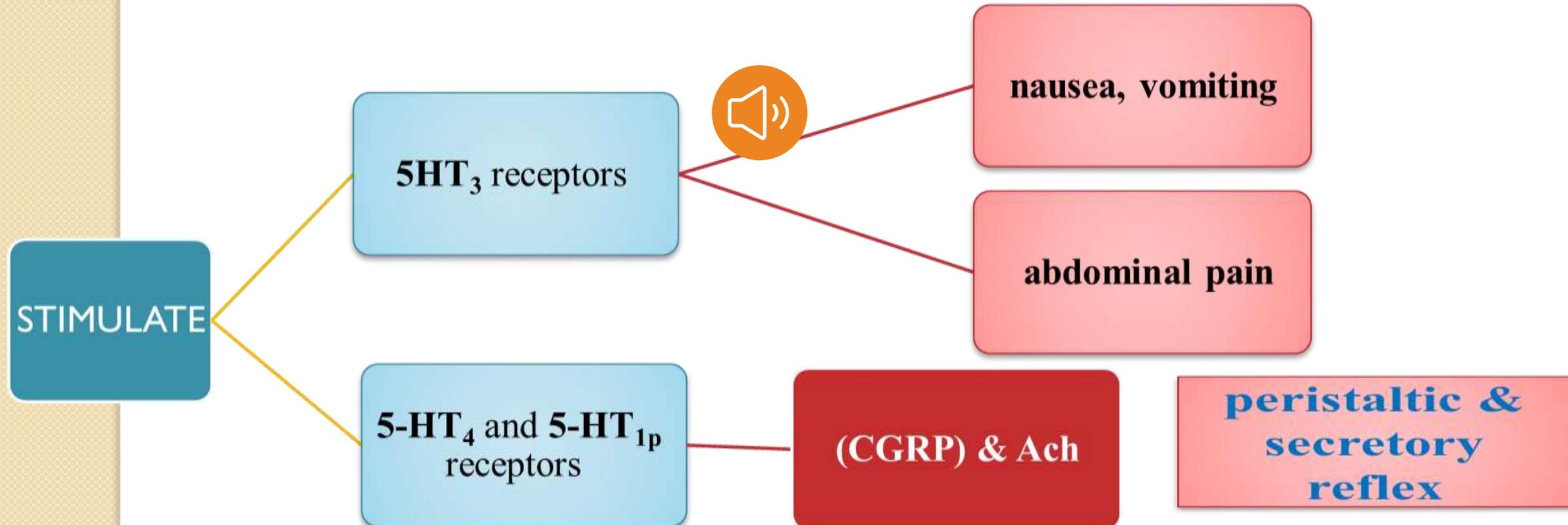


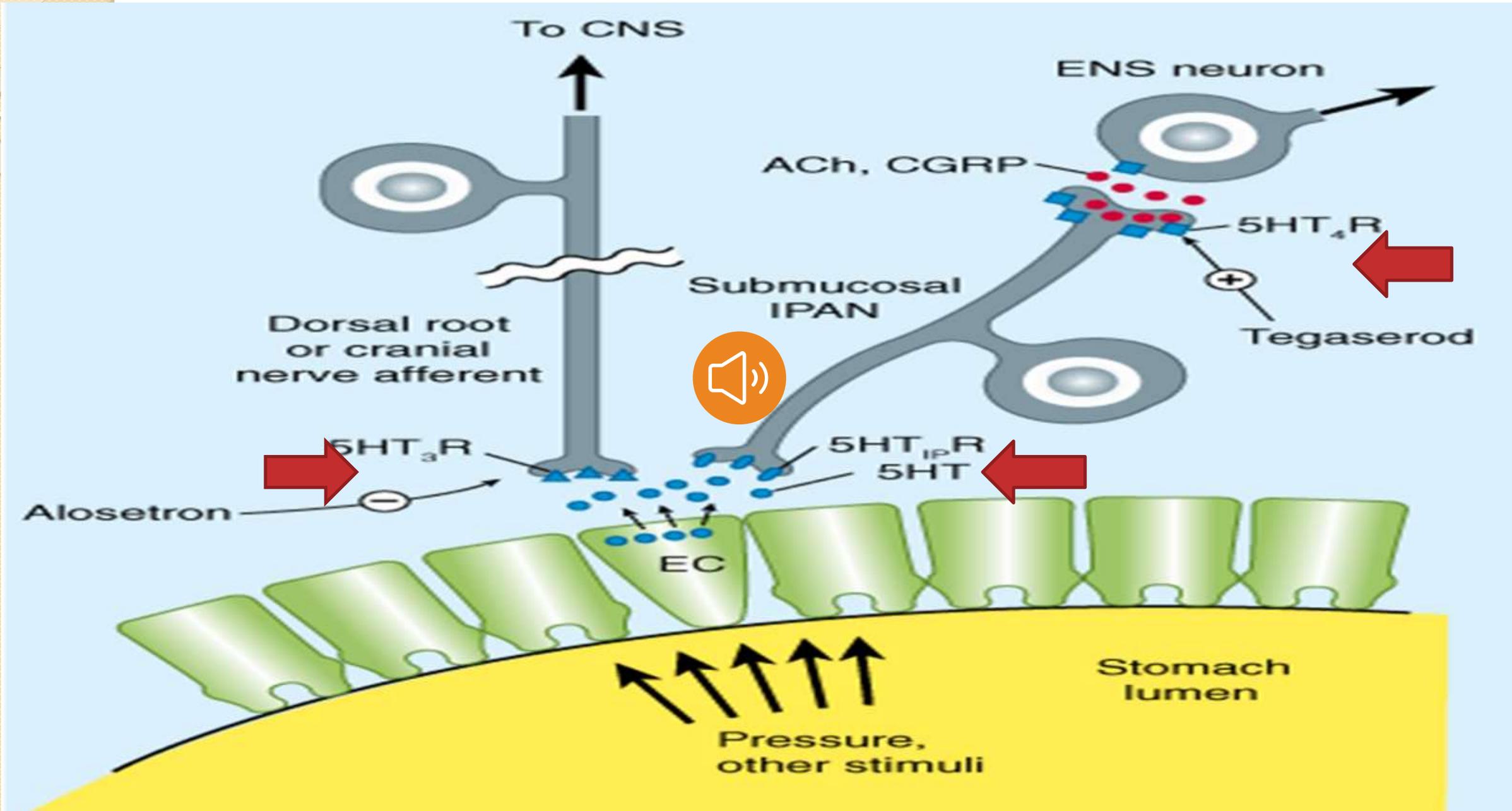
CALCITONIN GENE RELATED PEPTIDES

ACETYLCCKOLINE

SERETONIN

- plays a major regulatory role in the ENS.
- released from intestinal mucosa enterochromaffin cells (EC)

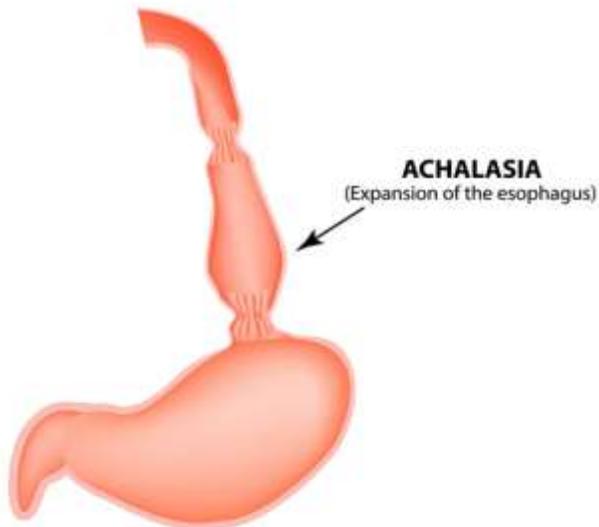




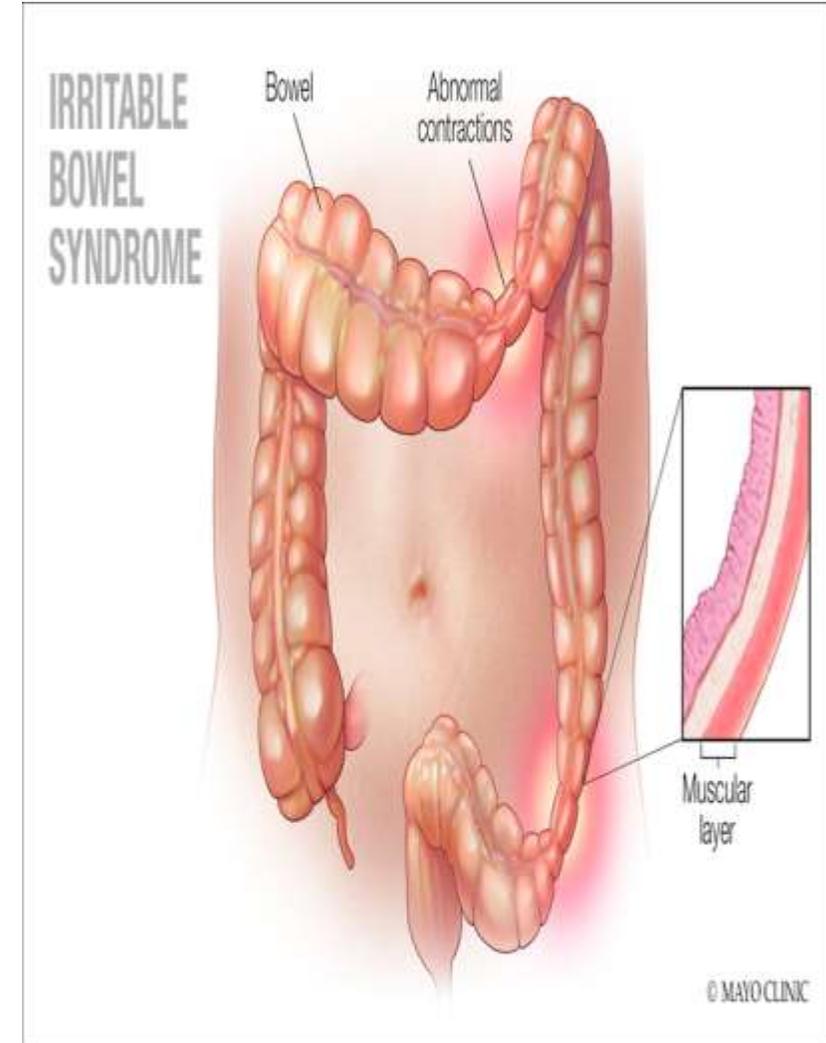
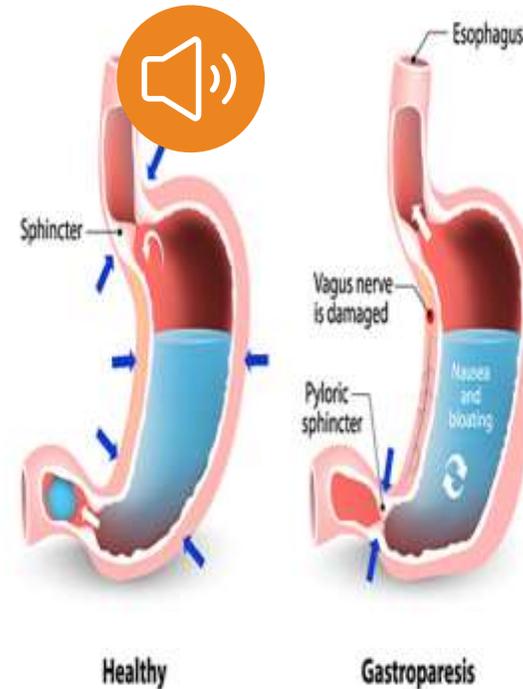
Motility disorders of the bowel:

1. Achalasia of the esophagus.
2. Gastroparesis.
3. Irritable bowel syndrome

ACHALASIA OF THE ESOPHAGUS



GASTROPARESIS



Prokinetic agents

- Drugs that selectively stimulate gut motor function.
- Drugs that improve gastric emptying may be helpful for gastroparesis & postsurgical gastric emptying delay.
- Agents that stimulate the small intestine may be beneficial for postoperative ileus or chronic intestinal pseudo-obstruction.
- Agents that enhance colonic transit may be useful in treatment of constipation



1-Dopamine (D₂) antagonists:

2.Serotonin receptor modulators

3-Cholinomimetic agent



4-macrolides

5-Chloride channel activator

Dopamine (D₂) antagonists

Metoclopramide

Domperidone

Sulpiride

Serotoninreceptor modulators

Tegaserod

Cisapride

Cholinomimetic agents

Bethanechol

Neostigmine

Macrolides

Erythromycin

Chloride channel activator

Lubiprostone



Metoclopramide (primperan)

- ➔ Mechanism of action:

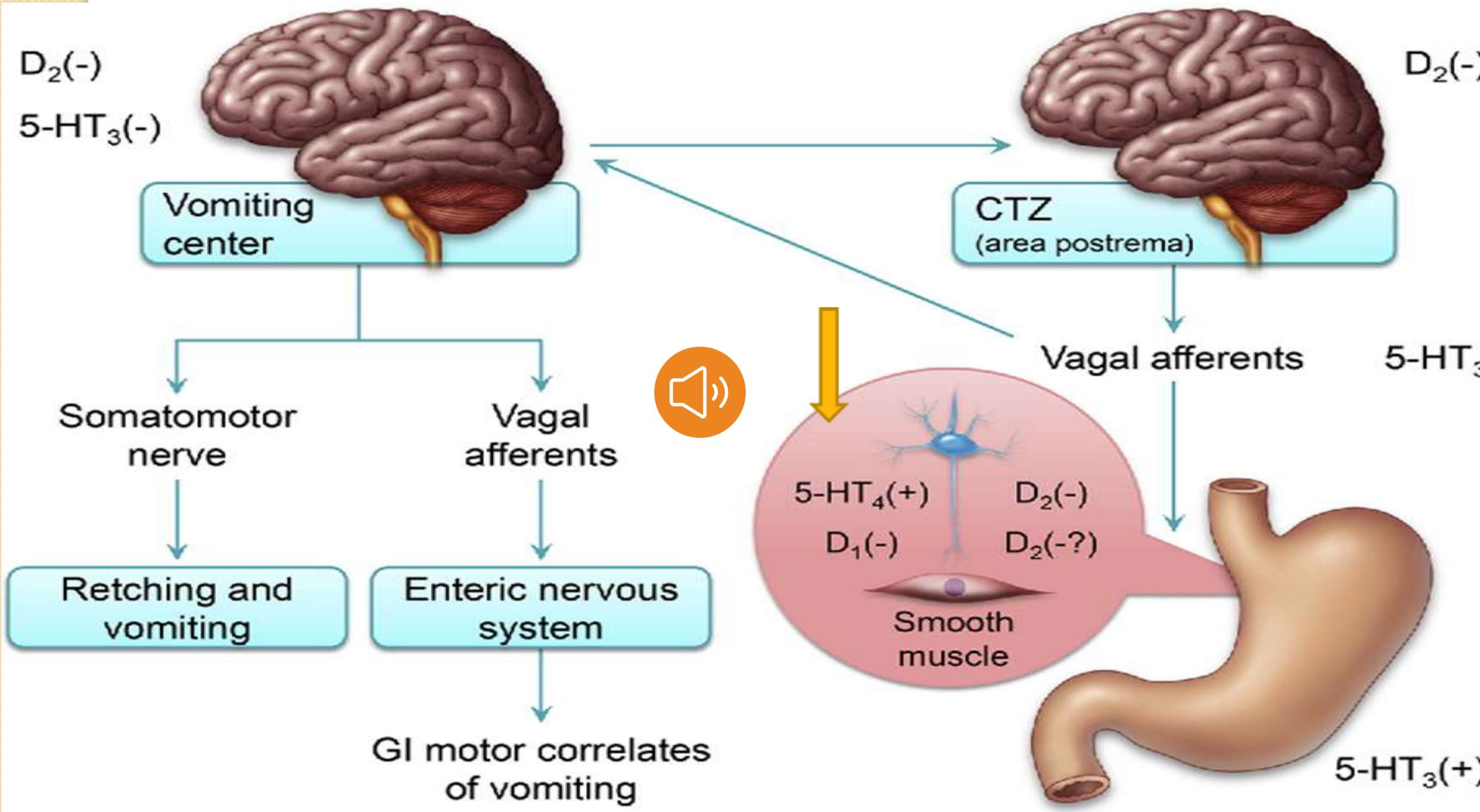
- ***D₂ receptor antagonist.***

- ***5-HT₄ agonist***

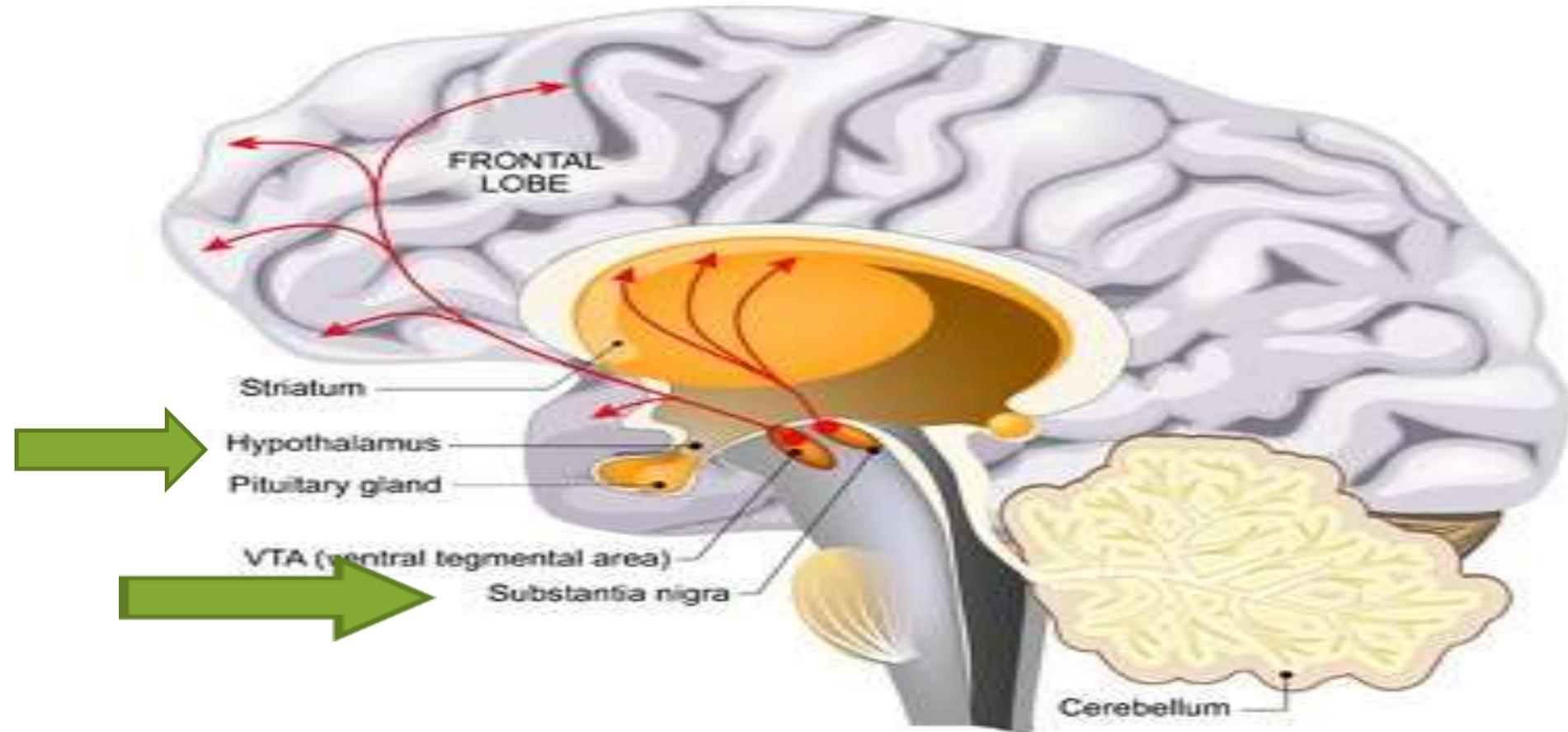
so ↑ release of Ach from myenteric plexus

- ***5-HT₃ antagonists.***





DOPAMINE PATHWAY



- ➔ Pharmacological effects:

- **I.C.N.S.:**

D₂-blocker. → A) Antiemetic. B) Hyperprolactinemia. C) Extrapiramidal



symptoms.

2.G.I.T.: ↑ esophageal peristaltic amplitude, ↑ LES, and enhances gastric emptying (upper digestive tract) but has no effect upon small intestine or colonic motility.

⇒ Pharmacokinetic:

- Rapidly absorbed.
- Half life 4-6 hrs.
- Distributed rapidly to most tissues (bi. brain barrier, placenta, milk).
- Hepatic metabolism (sulfation & glucuronidation).
- Excreted in urine



⇒ Uses:

1. Antiemetic (potent antiemetic).

2. Prokinetic action:

a. GERD (rarely used).

b. Hiccough.

c. Gastric hypomotility & postoperative ileus.

d. To facilitate intubation procedure (nasogastric feeding tube) and radiological examination of gut.

e. To empty the stomach before emergency surgery



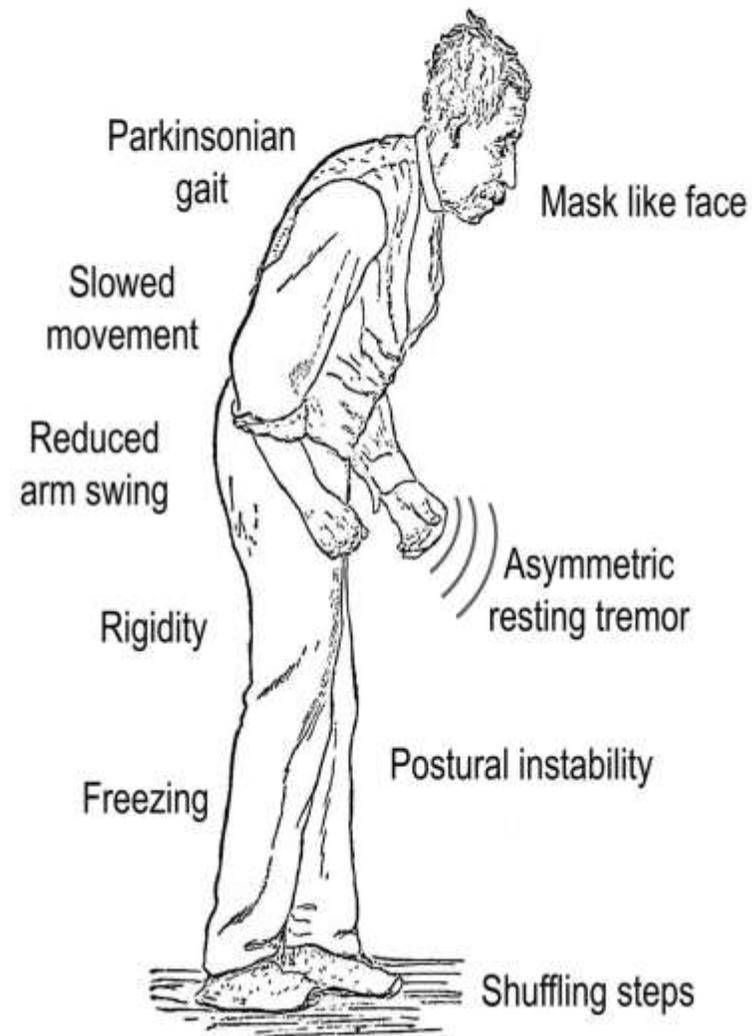
⇒ Side effects:

1. Restlessness, drowsiness, insomnia, anxiety & agitation (10-20%, especially the elderly).
2. **Extrapyramidal effects** (dystonia, akathisia, parkinsonian features).
 - 25% in high doses & 5% in long term therapy.
 - Tardive dyskinesia, sometimes irreversible (in long term therapy).
 - Long term use should be avoided unless absolutely necessary, especially in elderly.
3. Stimulates prolactin release → Galactorrhea, gynecomastia, impotence, menstrual disorders.



Akathisia:
 a movement disorder
 characterized by
 feeling of inner restlessness
 and inability to stay
 still.
 Often people feel
 like they want to
 crawl out of their
 own skin.

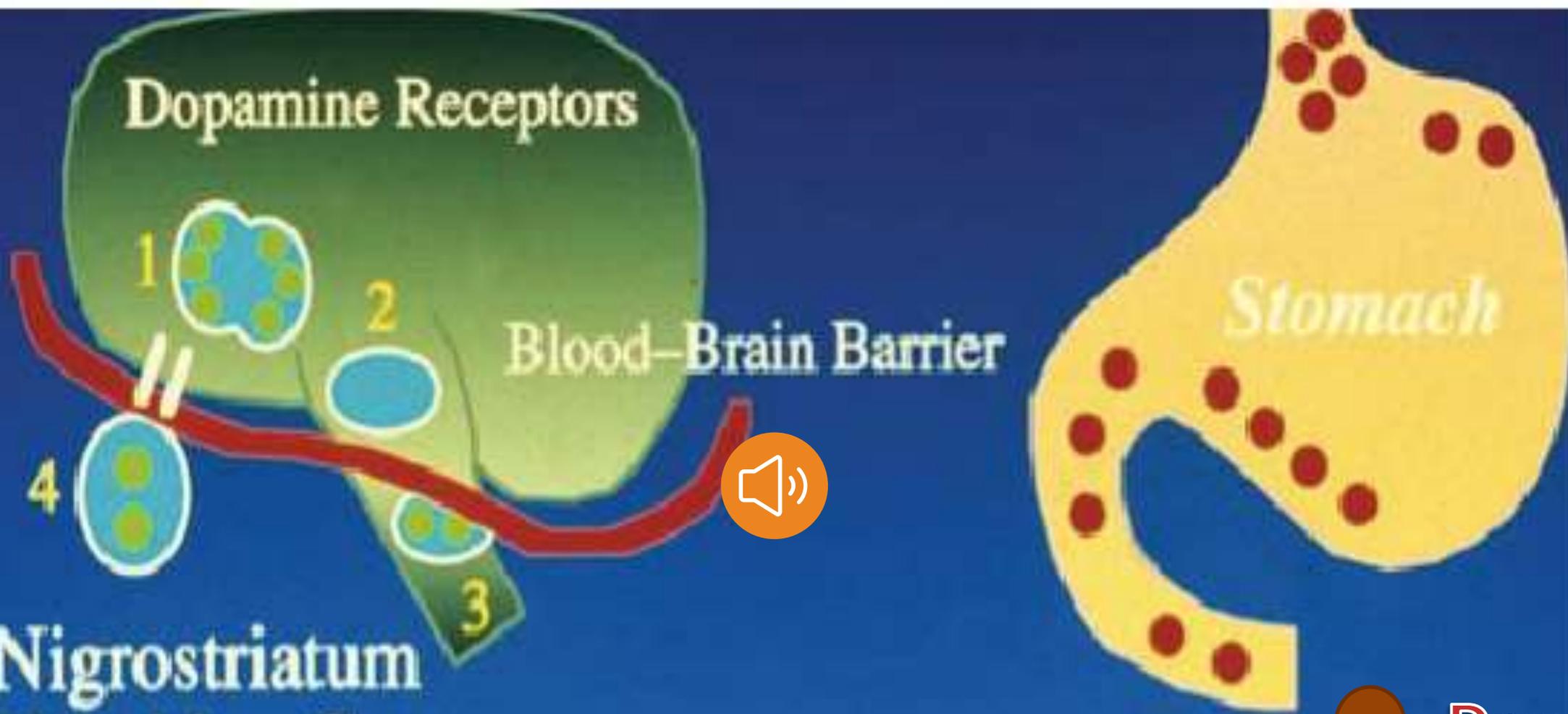
Parkinsonism



⇒ **Doses**: 10-20 mg orally or I.V. every 6hrs.

⇒ **Drug interactions**:

1. Short transit time in the stomach  → ↑ absorption of paracetamol
& ↓ absorption of digoxin.
2. Potentiates action of neuroleptics.
3. Antagonizes action of antiparkinsonian drugs.



Cisapride (prepulsid)

➔ Mechanism of action: 5HT₄ agonist (Release of myenteric Ach).

➔ Pharmacological effect: Acts on both upper and lower gut.

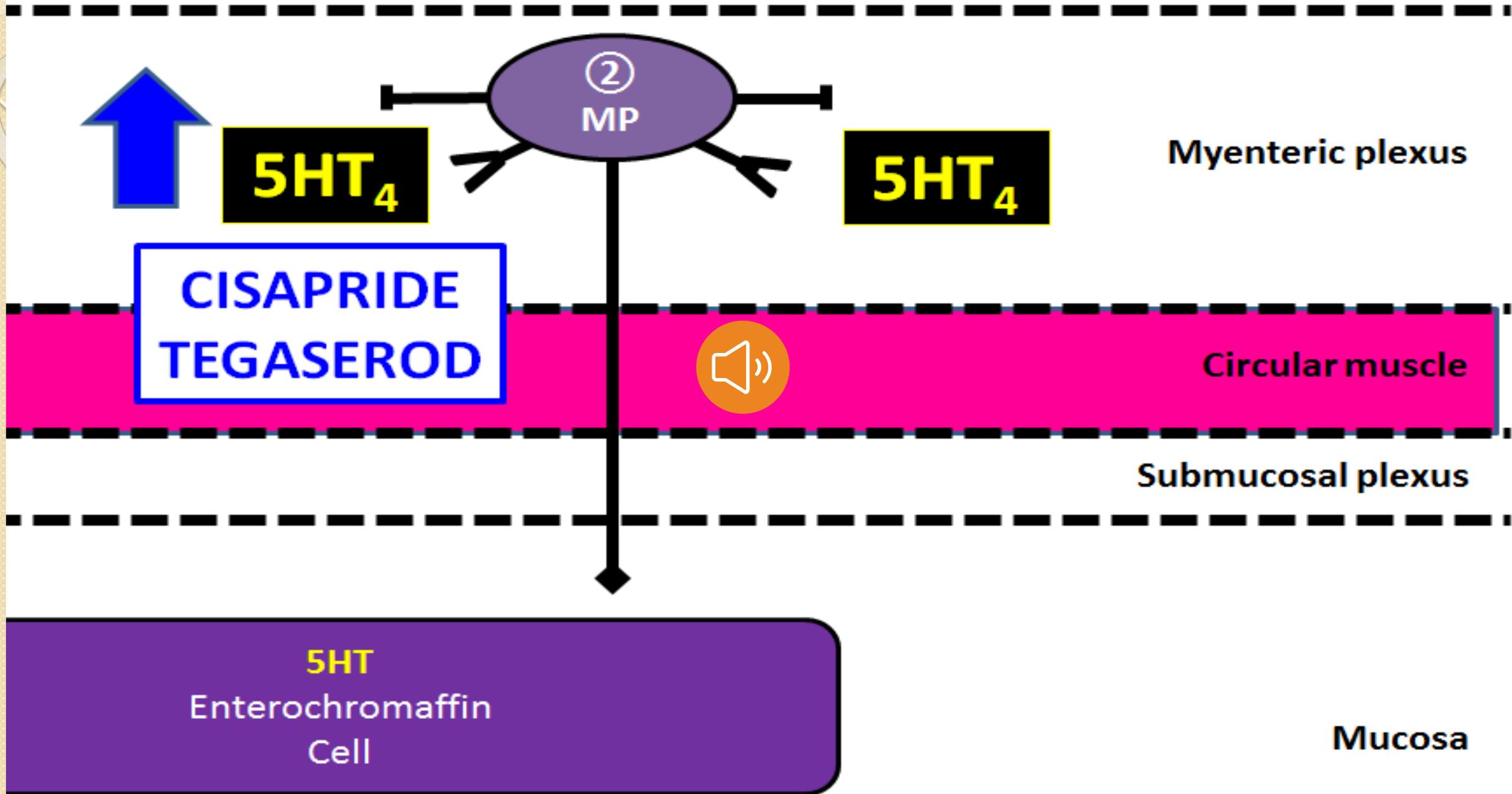
➔ Uses:

- Prokinetic.
- Chronic idiopathic constipation and colonic hypomotility.



➔ Side effects:

- Diarrhea.
- Arrhythmia (due to inhibition of cardiac K⁺ channels, which results in QT prolongation in some patients).



Macrolides

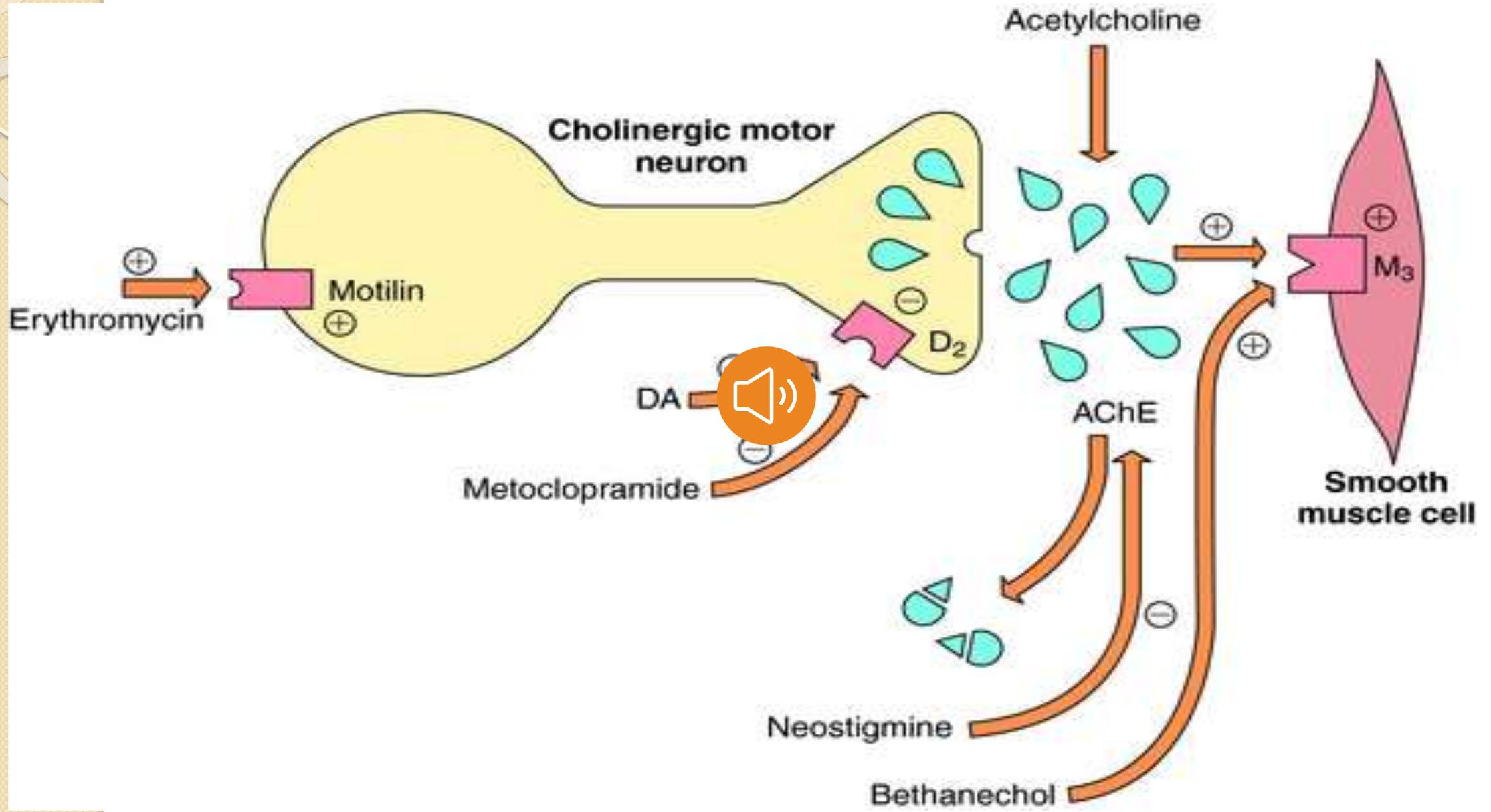
➔ Mechanism of action:

stimulate **motilin** receptors on G.I.T. smooth muscle & promote the onset of a migrating motor complex.



➔ Uses:

1. IV erythromycin in gastroparesis, however tolerance rapidly develops.
2. Acute upper GIT hemorrhage to promote gastric emptying of blood prior to endoscopy.



Chloride channel activator (Lubiprostone)

- **Mechanism of action:**

Acts by stimulating chloride channel

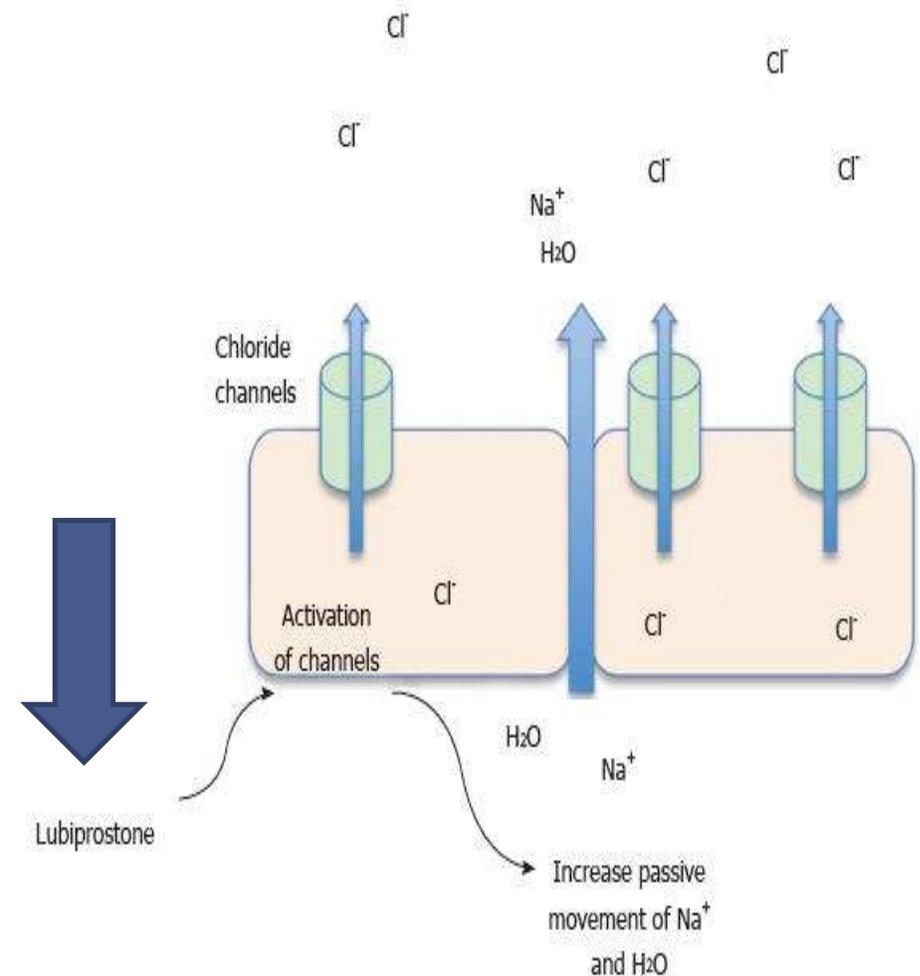
opening in the intestine → ↑ liq



secretion into the intestine &

shortens intestinal transit time.

- Used in chronic constipation





Thank
you!