

Unit V – Problem 3 – Pharmacology: Prokinetics

- Structure of the GIT (see the image).

- Prokinetics:

- **Definition:** they are drugs which enhance the gastrointestinal mobility by increasing the contractions.
- They stimulate gastric emptying (the process of propelling gastric contents to the small intestines) through:

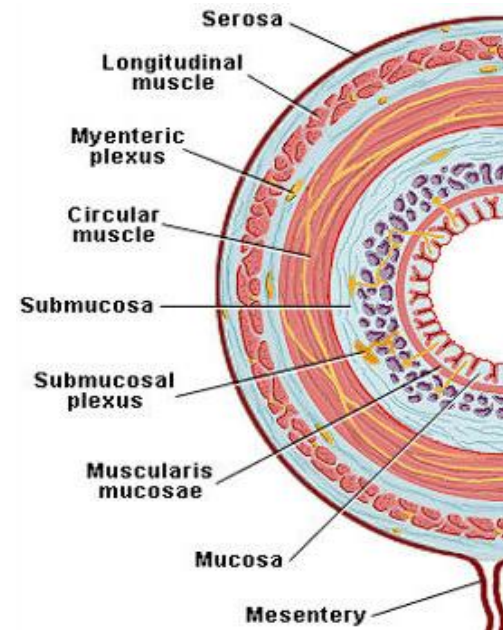
✓ Antagonism (opposition) of enteric dopamine D₂ receptor:

❖ Dopamine has an inhibitory effect on the mobility of GIT (it reduces the tone of LES & gastric contractions). Dopamine will bind to its receptor (dopamine D₂ receptor which is present on the myenteric plexus) and will inhibit the release of Ach from the plexus so the muscle fibers will not be stimulated.

❖ **Note:** myenteric plexus is neuronal cell bodies which are located between the inner circular and outer longitudinal muscle fibers of the muscularis propria layer in the GIT. This plexus causes contraction of the smooth muscles by releasing Ach.

✓ Agonism of serotonin (5HT) receptors (5HT₄).

❖ When the stomach is distended, EC (Enterochromaffin Cells) will release serotonin (5HT). Serotonin will bind to (5HT_{1P}R) found on the submucosal intrinsic primary afferent neurons (submucosal IPAN) and to (5HT₃ receptors) found on extrinsic primary afferent neurons. On the other end of the submucosal IPAN are (5HT₄ receptors) which if stimulated will cause the release of Ach thus enhancing the peristaltic and secretory activity.



Agent	Mode(s) of action	Physiologic effect	Adverse effect
DOPAMINERGIC * Metoclopramide	Dopamine D ₂ receptor antagonist Serotonin 5HT ₄ receptor agonist Serotonin 5HT ₃ receptor antagonist	Antiemetic Increasing LES tone Accelerating gastric emptying	Extrapyramidal side effects. Drowsiness. Hyperprolactinemia
* Domperidone	Dopamine D ₂ receptor antagonist	Antiemetic Increasing LES tone Accelerating gastric emptying	Hyperprolactinemia
SEROTONERGIC * Mosapride	Serotonin 5HT ₄ receptor agonist Serotonin 5HT ₃ receptor antagonist	Antiemetic Accelerating gastric emptying Increases gastric antral motility	-
* Tagoserod	Partial serotonin 5HT ₄ receptor agonist	Accelerating gastric emptying Increases gastric antral motility	-
MOTILIN (MACROLIDE ANTIBIOTICS) * Erythromycin	Motilin receptor agonist	Increasing LES tone Accelerating gastric emptying Accelerating gastric & small bowel contractility	-

