

Unit- 4

GIT Pharmacology-

Antiulcer drugs, Prokinetics, antiemetics, anti-diarrheals and drugs for constipation and irritable bowel syndrome

Chronopharmacology

Biological and circadian rhythms, Applications of chronotherapy in various diseases like

cardiovascular disease, diabetes, asthma and peptic ulcer

Prokinetics-

Prokinetics are a group of medications that help improve the movement of food through the digestive tract. They work by increasing the motility (movement) of the stomach and intestines, without causing diarrhea.

These drugs are mainly used to treat digestive problems such as:

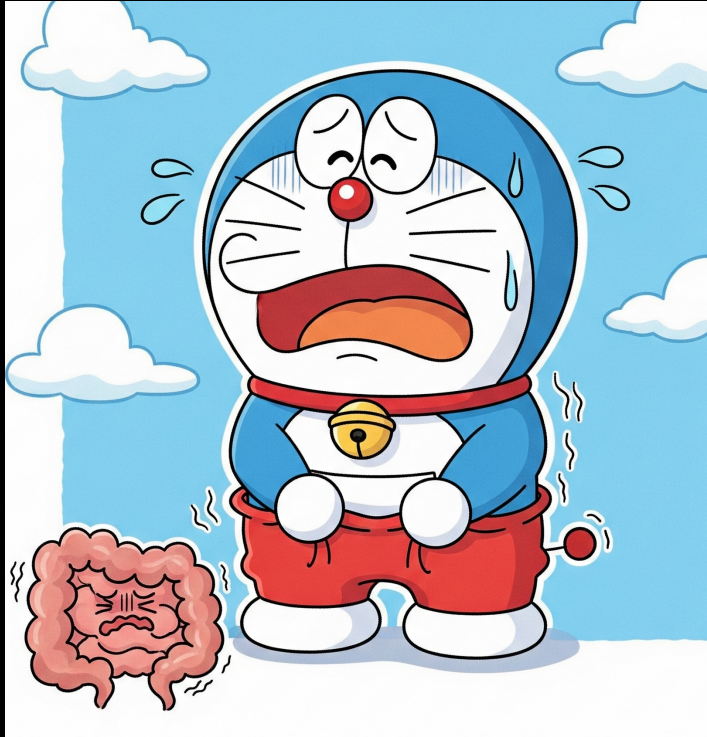
Gastroparesis (delayed stomach emptying)

Acid reflux (GERD)

Indigestion

They act by enhancing the action of acetylcholine or serotonin on the gut, which stimulates smooth muscle contractions.

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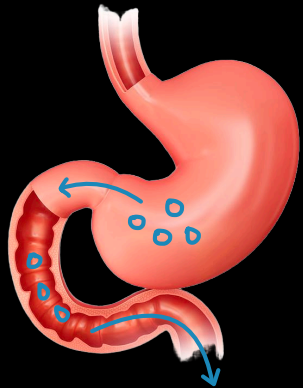


- Bloating (Gas).

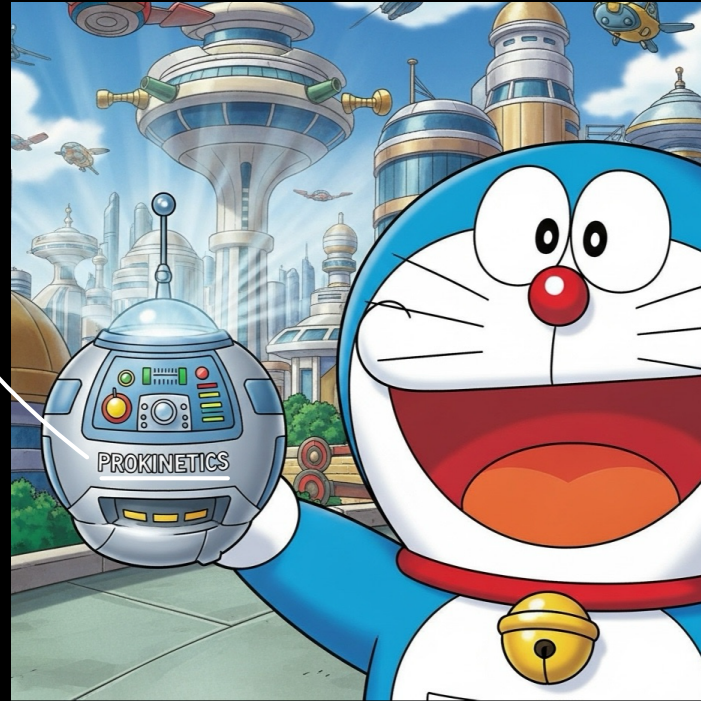
- Nausea

- Heartburn.

↳ Burning Sensation
in Chest.



Domperidone.

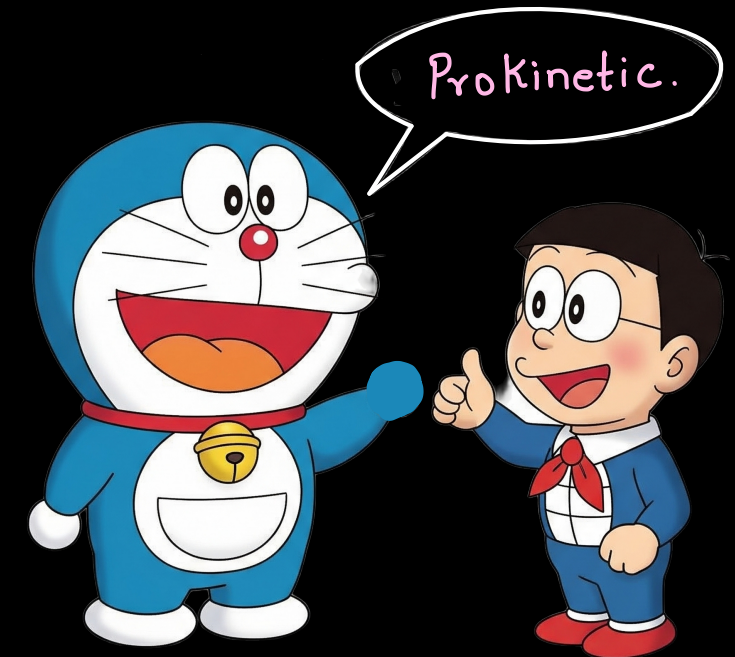


↳ Mainly Used to Treat.

-Gastroparesis (delayed
stomach emptying)

-Acid reflux (GERD)

-Indigestion



Ach



Serotonin.

Action Enhance on Gut.

Stimulate Smooth Muscle Contract.

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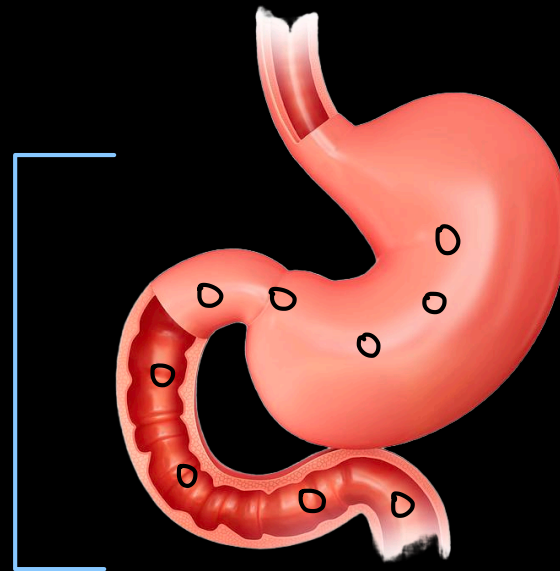


Dopamine

Release^x



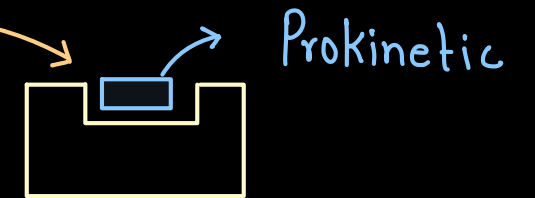
Smooth
Muscle Contract.



★ Ach help Intestine &
Stomach for Movement.

Prokinetic
↓

Block the Dopamine
Receptor.



↓
Dopamine
release

1. Dopamine D_2 Receptor Antagonism–

Drugs: Metoclopramide, Domperidone

Dopamine inhibits GI motility.

These drugs block dopamine D_2 receptors in the GI tract and brain.

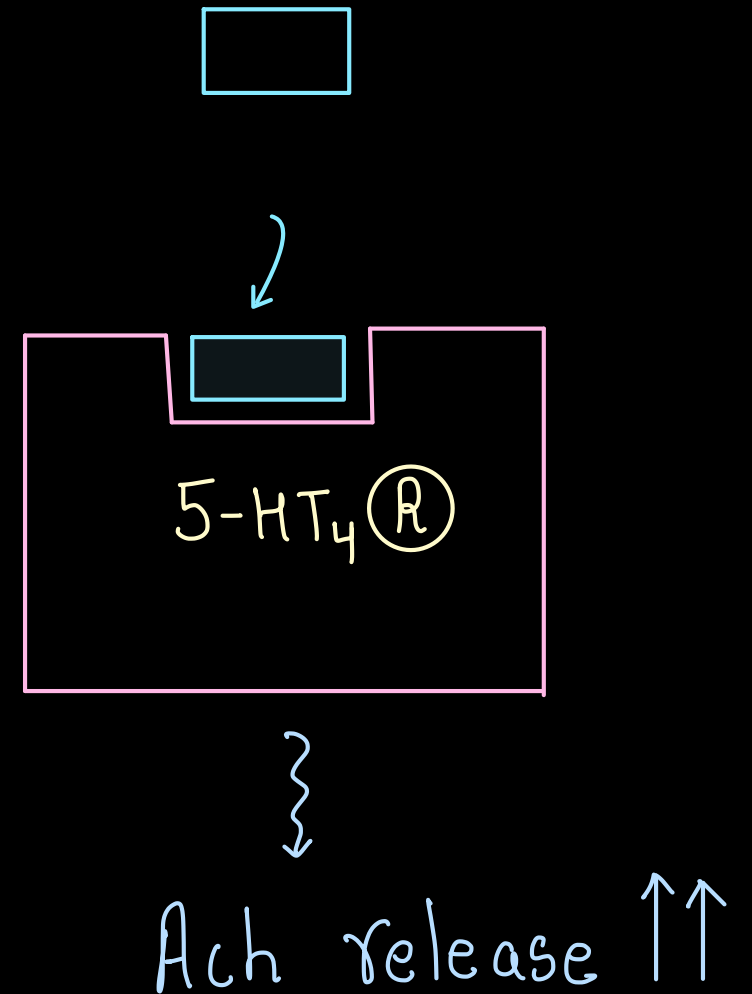
This removes the inhibitory effect of dopamine, allowing acetylcholine to work better, which increases GI movement.

2. 5-HT₄ Receptor Agonism

Drugs: Cisapride, Prucalopride

They stimulate serotonin (5-HT₄) receptors, which enhances acetylcholine release from enteric nerves.

Acetylcholine stimulates smooth muscle contraction and speeds up gastric emptying.

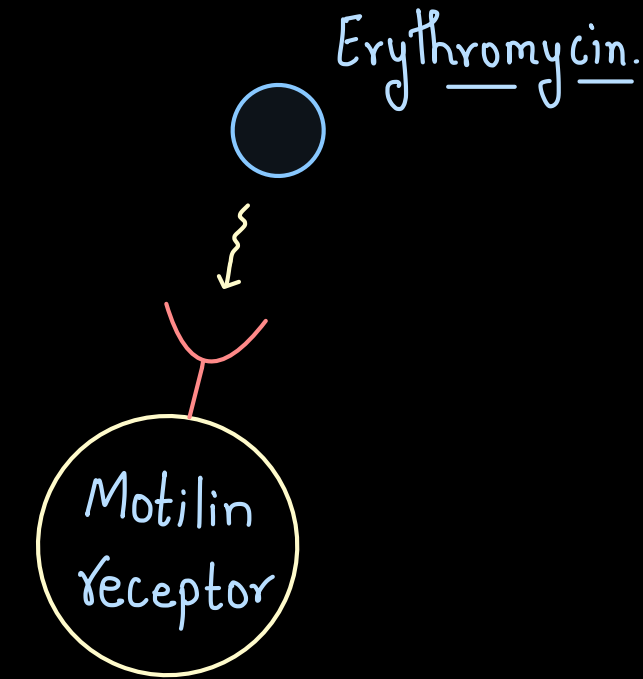


3. Motilin Receptor Agonism-

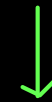
Drug: Erythromycin (at low doses)

Binds to motilin receptors in the stomach and small intestine.

This stimulates strong peristaltic waves that help clear the stomach.



Stomach, Small Intestine



Stimulate peristaltic wave
that help clear stomach.

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Side effects

1. Domperidone-

Does not enter the brain easily, so fewer brain side effects

But can affect the heart:

💖 QT prolongation (can cause abnormal heart rhythm)

😓 Dry mouth

😓 Headache

2. Erythromycin (used at low doses as prokinetic)-

Mainly causes:

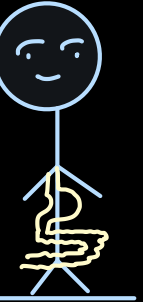


Nausea



Vomiting

Inflammatory Bowel Disease (IBD)



Inflammatory Bowel Disease (IBD) is a group of chronic (long-lasting) disorders that cause inflammation of the digestive tract, especially the intestines.

The two main types of IBD are:

Crohn's Disease

Ulcerative Colitis

1. Crohn's Disease

Can affect any part of the gastrointestinal (GI) tract — from mouth to anus.

-Involves all layers of the intestinal wall

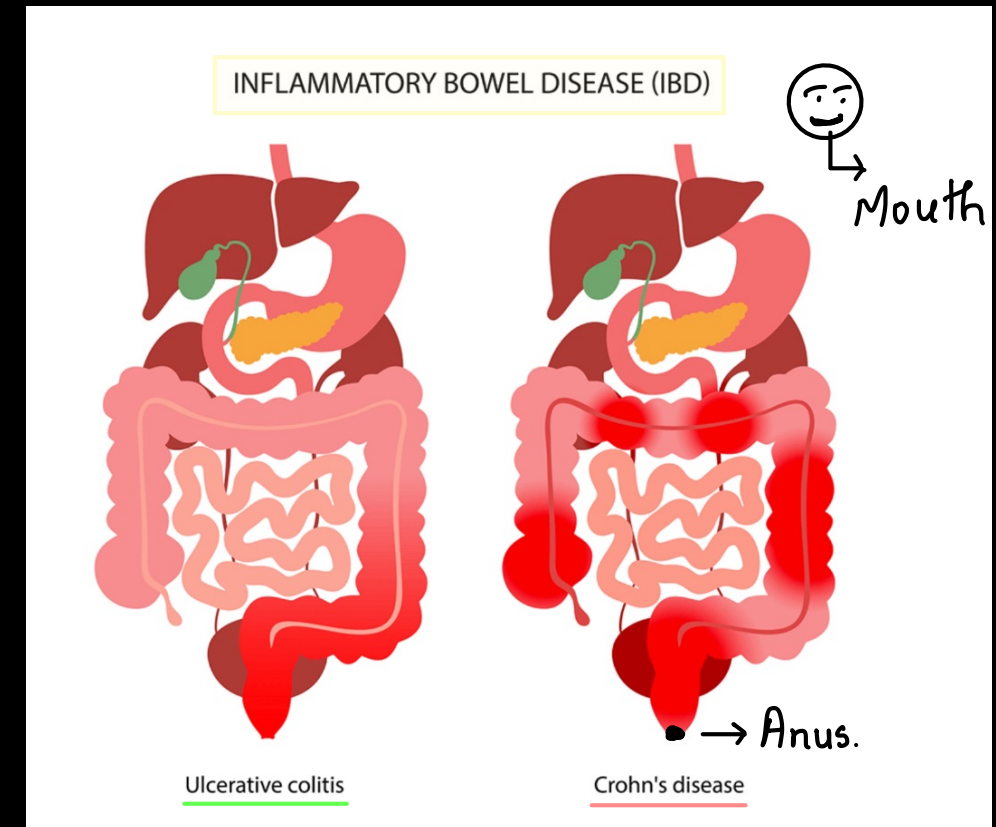
-Inflammation occurs in patches

2. Ulcerative Colitis-

-Affects only the colon (large intestine)

-Involves only the inner lining of the colon

-Inflammation is continuous, not patchy



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◆ Clinical Features / Symptoms

Common Symptoms	Ulcerative Colitis	Crohn's Disease
Diarrhea	Often with blood and mucus	May be non-bloody
Abdominal pain	Lower left side (common)	Lower right side (common)
Weight loss	Yes	Yes
Fatigue, fever	Yes	Yes
Urgency to pass stool	Common	Less common

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-Etiology / Causes of IBD -

Immune system dysfunction – abnormal immune response attacking the gut

Genetic factors – family history increases risk

Environmental triggers – infections, diet, smoking, pollution

Microbial imbalance – altered gut flora may trigger inflammation

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Complications-

Intestinal strictures or obstruction
Fistula formation (Crohn's)
Toxic megacolon (UC)
Malnutrition
Increased risk of colorectal cancer

Diagnosis-

Blood tests: Anemia
Stool tests: Rule out infection
Colonoscopy: Visual examination + biopsy
Imaging (CT/MRI): Especially for Crohn's disease

Diet & Lifestyle-

Avoid trigger foods (spicy, dairy, fiber during flare-ups)
High-protein
Quit smoking (especially in Crohn's)
Manage stress, maintain hydration

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◆ Treatment

Drug Type	Examples
Anti-inflammatory drugs	Mesalamine, Sulfasalazine
Corticosteroids	Prednisolone (short-term use)
Immunosuppressants	Azathioprine, Methotrexate
Biologics	Infliximab, Adalimumab (anti-TNF agents)
Antibiotics	For complications in Crohn's
Surgery	Required in severe/refractory cases

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Applications of chronotherapy

In various diseases like cardiovascular disease, diabetes, asthma and peptic ulcer

Chronotherapy means giving medicine at the right time of the day to make it work better and have fewer side effects.

🕒 Because our body has a natural clock (called the circadian rhythm), different body functions work differently in the morning, afternoon, and night.

✅ **Why is timing important?**

Your body changes throughout the day:

Blood pressure is high in the morning

Asthma gets worse at night , Stomach acid increases at night

CHRONOTHERAPY

Give medicine at the right time of day to work better and have fewer side effects.

DISEASE	WHEN TO GIVE MEDICINE	REASON
CARDIOVASCULAR DISEASE	At NIGHT	To stop high BP in the morning (heart attack risk)
ASTHMA	In the EVENING/NIGHT	Because breathing problems are worse at night
DIABETES	BEFORE MEALS	To control sugar when you eat
PEPTIC ULCER	BEFORE SLEEPING	Because stomach acid is more at night



1. Cardiovascular Disease–

(Examples: Hypertension, Heart Attack, Stroke)



What happens in the body?

Our blood pressure (BP) naturally increases early in the morning (around 4–6 AM)

This is due to the body's circadian rhythm activating stress hormones (like cortisol and adrenaline)

Most heart attacks and strokes happen in the early morning because of this BP surge



Chronotherapy approach:

Take antihypertensive medicines at night (bedtime dosing)

Why night is better?

Controls the early morning BP rise

Protects the heart and brain during high-risk hours

Improves 24-hour BP control

Examples of drugs:

ACE inhibitors (e.g., enalapril)

ARBs (e.g., losartan)

Calcium channel blockers (e.g., amlodipine)

Beta blockers (e.g., atenolol)

2. Asthma-

 What happens in the body?

Lung function is naturally lower at night

Airways become more inflamed and narrow during sleep

Asthma symptoms like wheezing, coughing, breathlessness are worse between midnight and 6 AM

 Chronotherapy approach:

Take asthma medications in the evening or at bedtime

 Why night dosing is better?

Prevents nighttime attacks

Improves lung function during sleep

Reduces need for emergency inhaler at night

Examples of drugs:

Inhaled corticosteroids
(e.g., budesonide, fluticasone)

Long-acting bronchodilators
(e.g., salmeterol)

Theophylline (slow-release at night)

3. Diabetes Mellitus–

🕒 What happens in the body?

Blood glucose levels rise after meals, especially in the morning (due to insulin resistance at that time)

Body's insulin action also varies with the circadian rhythm

💊 Chronotherapy approach:

Take oral antidiabetic drugs or insulin before meals, particularly before breakfast and dinner

✅ Why this timing helps?

Matches insulin or drug action with meal-related sugar spikes

Prevents post-meal hyperglycemia

Reduces risk of complications (retinopathy, nephropathy)

Examples of drugs:

Metformin – usually taken with meals

Insulin – timed around meals

Glipizide, Gliclazide – taken 30 min before food

🤔 4. Peptic Ulcer Disease

🕒 What happens in the body?

Stomach acid secretion is highest during the late evening and night

At night, acid damages the stomach or duodenum lining, worsening ulcers

Night-time pain is common in peptic ulcers

💊 Chronotherapy approach:

Take acid-suppressing drugs at bedtime

✅ Why night dosing is better?

Reduces acid during the most damaging time (night)

Promotes healing of the ulcer

Relieves nighttime pain and discomfort

Examples of drugs:-

Proton pump inhibitors (PPIs):

Omeprazole, Pantoprazole

H2 blockers: Ranitidine,

Famotidine (often used at night)