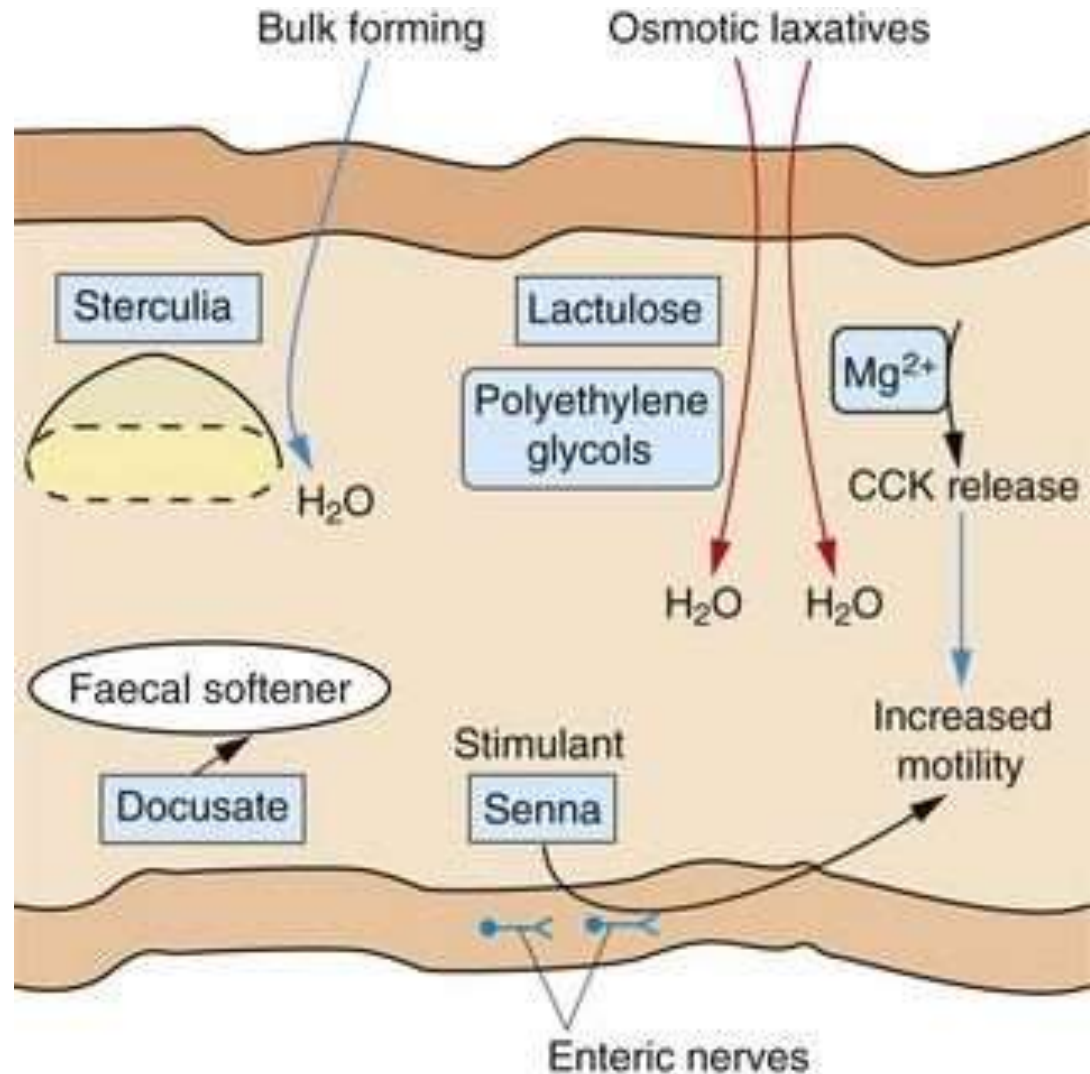


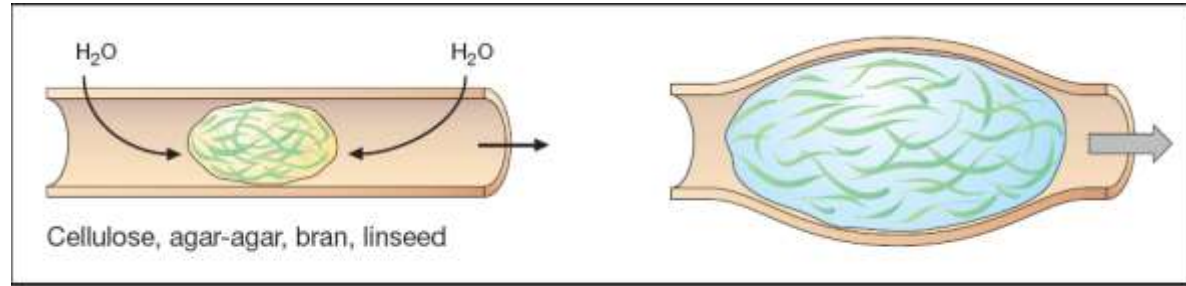
Laxatives

Intermittent constipation is best prevented with:
a high-fiber diet.
adequate fluid intake.
responding to nature's
Call.
Regular exercise.

CCK: cholecystokinin



Bulk-Forming Laxatives



B. Bulk laxatives

Indigestible, hydrophilic colloids that absorb water, forming a bulky, emollient gel that distends the colon and promotes peristalsis.

Effective within 1-3 days.

Common preparations include natural plant products (**psyllium, methylcellulose, bran**) and synthetic fibers (**polycarbophil**).

Bacterial digestion of plant fibers within the colon may lead to increased **bloating and flatus**.

Stool Surfactant Agents (Softeners)

Docusate

Detergents or surfactants that act as stool-wetting and stool-softening agents, allowing the mixing of water, lipids, and fecal matter.

Alters intestinal permeability and increases net water and electrolyte secretions in the intestine.

Orally: Softening of feces within **1-3 days**

Rectally: effective within **5 to 20 minutes**.

Used in symptomatic treatment of constipation & in painful anorectal conditions such as hemorrhoids and anal fissures.

Glycerin suppository.

works by irritating the lining of the intestine and increasing the amount of fluid, making it easier for stools to pass.

Lubricant/Emollient

Site of Action: **Colon.**

Onset of Action: 6 - 8 hours.

Causing lubrication of the stool & make it slippery, so that it slides through the intestine more easily.

It is not absorbed and increase the bulk of the intestinal contents as it reduces the water absorption

Liquid paraffin

Used to prevent and treat fecal impaction.

Aspiration can result in a severe lipid pneumonitis

Long-term use can impair absorption of fat-soluble vitamins.

Can slip out of anal sphincter and causes embarrassment. Not recommended for regular use.

Osmotic Laxatives

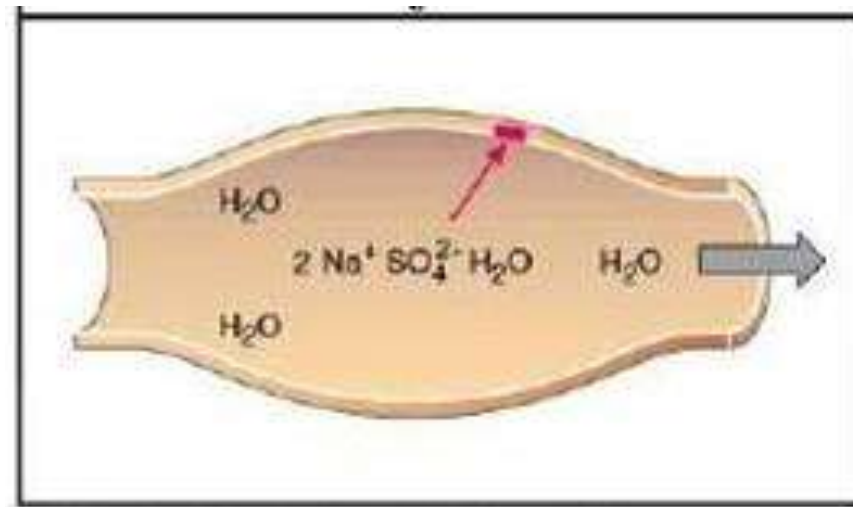
Soluble but nonabsorbable compounds that result in increased stool liquidity due to an increase in fecal fluid.

Nonabsorbable Sugars or Salts

Magnesium hydroxide (milk of magnesia)

Not used for prolonged periods in renal insufficiency due to the risk of hypermagnesemia.

Large doses of **magnesium citrate & sodium phosphate** cause Purgation: rapid bowel evacuation within 1-3 h. This might cause volume depletion.



C. Osmotically active laxatives

Lactulose

Disaccharide, not absorbed causing retention of water through osmosis leading to softer, easier to pass stool.

in the **colon**, it is **fermented** by the gut flora producing osmotic metabolites causing **severe flatus and cramps**.

Drug of choice in **hepatic encephalopathy** to trap NH_3 .

Lactulose is converted into lactic acid, which decreases the luminal pH. So, NH_3 is trapped and prevented from absorption.

Balanced Polyethylene Glycol:

Safe solution: no intravascular fluid or electrolyte shifts.

Does not cause cramps or flatus.

It is a laxative solution that increases the amount of water in the intestinal tract to stimulate bowel movements.

PEG is an inert, nonabsorbable, cosmetically active sugar.

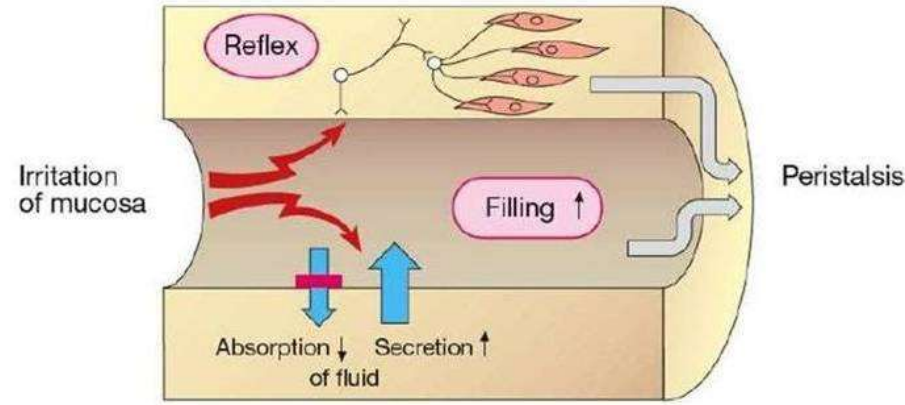
It also contains Sodium sulfate, bicarbonate and potassium chloride to replace electrolytes that are passed from the body in the stool used to clean the bowel before colonoscopy, a barium x-ray or other intestinal procedures.

For colonic cleansing, it is ingested rapidly (4L over 2-4 h).

For chronic constipation, PEG powder is mixed with water or juice.

Stimulant Laxatives

Direct stimulation of the enteric nervous system and colonic electrolyte and fluid secretion.



Anthraquinone Derivatives:

Aloe, senna, and cascara

Occur naturally in plants.

Poorly absorbed & after hydrolysis in the colon, produce a bowel movement in 6–12 h when given orally and within 2 h when given rectally.

Chronic use leads to a brown pigmentation of the colon known as "**melanosis coli.**"

Bisacodyl

Tablet and suppository for treatment of acute and chronic constipation

induces bowel movement within 6–10 h orally and 30–60 minutes rectally.

Safe for acute and long-term use

Phenolphthalein

Removed from the market owing to concerns about possible cardiac toxicity.

Castor Oil

Hydrolyzed in upper intestine into ricinoleic acid which is a local irritant.

Was used as purgative to clean the colon before procedures.

Opioid Receptor Antagonists

Do not cross the BBB.

Block peripheral (μ) mu – opioid receptors without central analgesic effects.

Methylnaltrexone

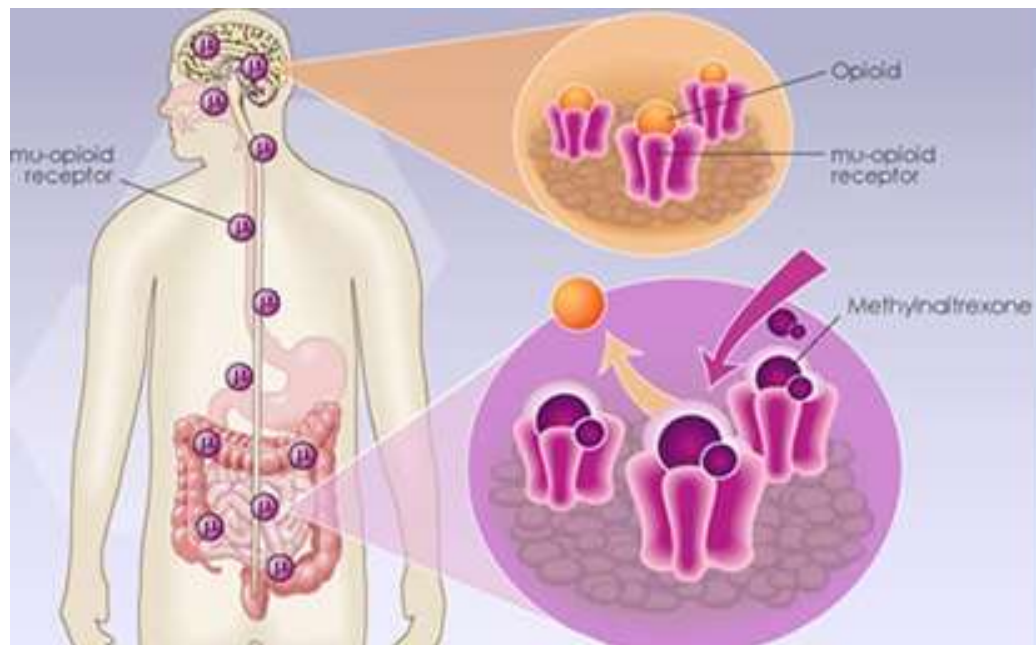
Used for opioid - induced constipation in patients with advanced illness

not responding to other agents. S.C. injection every 2 days.

Alvimopan

Short-term use for postoperative ileus in hospitalized patients.

Given orally within 5 hours before surgery and twice daily after surgery until bowel function has recovered, but for no more than 7 days, because of possible cardiovascular toxicity.



Antidiarrheal Agents

Should not be used in patients with **bloody diarrhea, high fever, or systemic toxicity** because of the risk of worsening the underlying condition.

Used to control chronic diarrhea caused by **irritable bowel syndrome (IBS)** or **inflammatory bowel disease**.

Opioid Agonists

Increase colonic transit time and fecal water absorption.

They also decrease mass colonic movements

CNS effects and potential for addiction limit the usefulness of most.

Loperamide

Does not cross BBB, so No analgesic or addiction potential.

Diphenoxylate

Not analgesic in standard doses.

Higher doses have CNS effects.

Can cause dependence.

Commercial preparations contain small amounts of **atropine**

Lomotil Diphenoxylate and Atropine which contribute to the antidiarrheal action.

Bile Salt-Binding Resins

Cholestyramine

Colestipol

Colesevelam

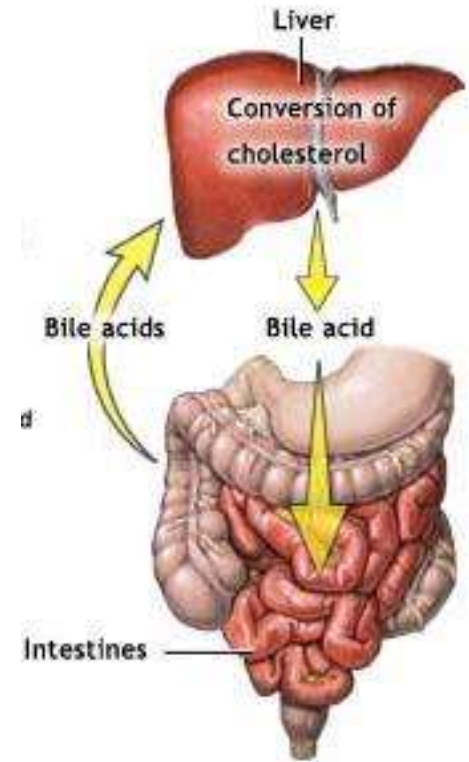
Malabsorption of bile salts cause diarrhea.

(**Crohn's disease or after surgical resection**),

They bind bile salts and decrease diarrhea caused by excess fecal bile acids.

Can cause bloating, flatulence, constipation and fecal impaction.

Cholestyramine and **colestipol** reduce absorption of drugs and fat, but **Colesevelam** does not.



Octreotide:

Synthetic octapeptide with actions similar to somatostatin.

Clinical Uses:

1. Inhibition of endocrine tumor effects:

Carcinoid and VIPoma (neuroendocrine tumors that secrete vasoactive intestinal polypeptide (VIP)) can cause secretory diarrhea, flushing and wheezing.

2. Diarrhea due to vagotomy or dumping syndrome (ingested foods bypass the stomach too rapidly) or short bowel syndrome and AIDS.

3. To stimulate motility in small bowel bacterial overgrowth or intestinal pseudo-obstruction secondary to scleroderma (a disease affecting the skin and other organs that is one of the autoimmune rheumatic diseases).

4- It inhibits pancreatic secretion, so used in patients with pancreatic fistula (leakage of pancreatic secretions from damaged pancreatic ducts).

5- treatment of pituitary tumors (e.g., acromegaly)

6- Sometimes used in gastrointestinal bleeding.

Adverse Effects:

Impaired pancreatic secretion may cause **steatorrhea** which can lead to fat-soluble vitamin deficiency.

Nausea, abdominal pain, flatulence, and diarrhea.

Formation of sludge or **gallstones**, because of inhibition of gallbladder contractility and fat absorption.

Hyper or hypoglycemia due to hormonal imbalance.

Hypothyroidism.

Bradycardia.