

Drugs used in treating constipation and IBS

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What is constipation?



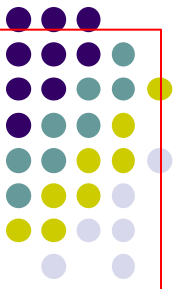
- infrequent defecation, often with straining and the passage of hard, uncomfortable stools.
- **May be accompanied by other symptoms:**
 - 👉 Loss of appetite
 - 👉 Flatulence
 - 👉 Abdominal and rectal pain
 - 👉 Lethargy
 - 👉 Depression

Causes of constipations



- **Decreased motility in colon:**
 - Decrease in water and fiber contents of diet.
- **Difficulty in evacuation:**
 - Local painful conditions: anal fissures, piles
 - Lack of muscular exercise
- **Drug-induced:**
 - Anticholinergic agents
 - Opioids
 - Iron
 - Antipsychotics

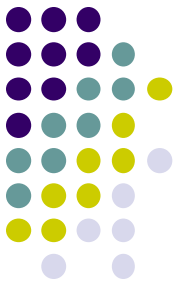
Treatment of Constipation



General Measures :

1. Adequate **fluid intake**
2. **High fiber** contents in diet
3. Regular exercise
4. Regulation of bowel habit
5. Avoid drugs causing constipation
6. Use drugs (**laxatives** or **purgatives**): **Drugs that hasten the transit of food through the GIT.**

Classification of laxatives or purgatives



I) Bulk forming laxatives:

Increase volume of non-absorbable solid residue.

II) Osmotic laxatives:

Increase water content in large intestine.

Classification of laxatives or purgatives



III) Stimulant or irritant laxatives:

Act by direct stimulation of nerve endings in colonic mucosa.

IV) Stool softeners (lubricants):

Alter the consistency of feces → easier to pass.

I- Bulk (fiber) Laxatives



Include:

Dietary fibers:

- **Indigestible parts of vegetables & fruits**
- **Bran powder**

Hydrophilic colloids

- **Psyllium seed**
- **Methyl cellulose**
- **Carboxymethyl cellulose (CMC)**

Mechanism of Action



Dietary fibers & hydrophilic colloids are non absorbable substances → Increase the **bulk of intestinal contents by water retention → ↑ mechanical pressure on the walls of intestine → stimulation of stretch receptors → ↑ peristalsis → evacuation of **soft** stool.**

Side Effects



- **Delayed onset of action (1-3 days).**
- **Intestinal obstruction (should be taken with enough water).**
- **Bloating, flatulence, distension**
- **Interfere with other drug absorption e.g. iron, cardiac glycosides.**

II- Osmotic Laxatives



- are water soluble compounds
- Poorly absorbable compounds (salts or sugars)
- They remain in the bowel, attract & retain water by **osmosis** thereby increasing the volume of feces → ↑ peristalsis → evacuation of stool.

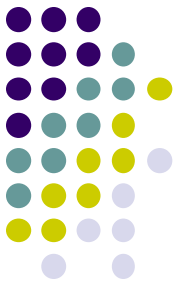
Osmotic Laxatives



Include:

1. **Sugars : e.g. lactulose**
2. **Salts (Saline laxatives)**
 - **Magnesium sulphate or hydroxide**
 - **Sodium or potassium phosphate**
3. **Polyethylene glycol (PEG)**

Lactulose



- Semisynthetic **disaccharide** of fructose & galactose
- Non absorbable
- **In colon**, metabolized by bacteria into fructose & galactose
- These sugars are fermented into lactic acid & acetic acid that function as **osmotic laxatives**.

Uses

- **Prevention of chronic constipation**
- **Hepatic encephalopathy (Hyperammonemia)**
- **Hemorrhoids**



Lactulose increases the H^+ concentration in the gut, This favors the formation of the non-absorbable NH_4^+ from NH_3 , trapping NH_3 in the colon & reducing its back diffusion into blood.

Why lactulose is commonly used in liver cirrhosis?

Mechanism:

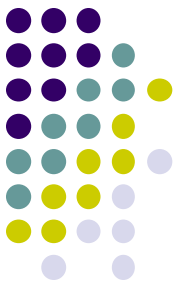
Lactulose \longrightarrow Lactic acid + Acetic Acid

\longrightarrow acidification of the colon \longrightarrow  ammonia

absorption (NH_4^+)

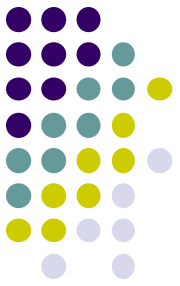
Dose:

15 ml for constipation and 30 ml for liver cirrhosis



Side Effects

1. **Delayed onset of action (2-3 days)**
2. **Abdominal cramps & flatulence**
3. **Electrolyte disturbances.**



Saline Laxatives



- Are poorly absorbable salts
- Increase evacuation of **watery** stool
- Magnesium sulphate (**Epson's salt**)
- Magnesium hydroxide (**milk of magnesia**)
- Sodium phosphate or potassium phosphate
- have rapid effect (**within 1-3 h**)
- Isotonic or hypotonic solution should be used

Uses

Treatment of acute constipation.



Side Effects

- **Disturbance of fluid & electrolyte balance**
- **May have systemic effects.**

Contraindications

Sodium salts in congestive heart failure

Magnesium salts are contraindicated in:

- **Renal failure**
- **Heart block**
- **CNS depression**
- **Neuromuscular block.**

Balanced Polyethylene Glycol (PEG)



- **Isotonic solution of polyethylene glycol & electrolytes (NaCl, KCl, Na bicarbonate)**
- **Is a colonic lavage solution**
- **Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours).**

Advantages

- **Limited fluid or electrolyte imbalance**
- **less flatulence and cramps.**

III- Stimulant Laxatives



are the most powerful group among laxatives & should be used with care.

Mechanism of Action:

act via direct stimulation of enteric nervous system → increased peristalsis & purgation.

Drugs

- **Bisacodyl**
- **Castor oil**
- **Anthraquinone derivatives (senna, cascara, aloes).**

Bisacodyl

Is given orally, acts on colon

Onset of action = orally (6-12 h)/ per rectum (1 h)



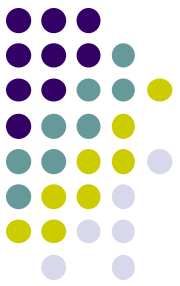
Castor Oil

- **Given orally**
- **5-20 ml on empty stomach in the morning**
- **acts in small intestine**
- **Vegetable oil degraded by lipase → ricinoleic acid + glycerin**
- **Ricinoleic acid is very irritating to mucosa.**
- **Onset of action = 2-6 h.**

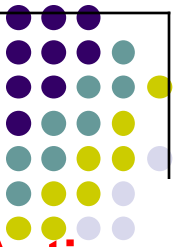
Anthraquinone glycosides

e.g. senna, cascara, aloe vera

- **Act in colon**
- **Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action).**
- **Emodin may pass into milk.**
- **Delayed onset of action (8-12 h).**
- **Bowel movements in 12 h (orally) or 2 h (rectally as suppository)**
- **Given at night.**



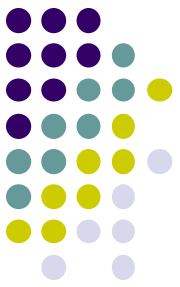
Common stimulant purgatives



Drugs	Type	Site of Action	Onset of Action
Cascara	Anthraquinone	colon	8-12 hours
Senna	Anthraquinone	colon	8- 12 hours
Aloe vera	Anthraquinone	colon	8-12 hours
Bisacodyl	Diphenylmethane	colon	6-8 hours
Castor Oil	ricinoleic acid	small intestine	2-6 hours

Side Effects

- **Abdominal cramps may occur**
- **Prolonged use → dependence & destruction of myenteric plexus leading to **atonic colon**.**



Contraindications

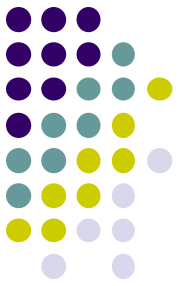
- **Senna is contraindicated in breast feeding**
- **Castor oil # in pregnancy → reflex contraction of uterus → abortion.**

Fecal Softeners (Lubricants)/surfactants



- **Are non absorbed drugs**
- **Act by either decreasing surface tension or by softening the feces thus promoting defecation.**
- **Treat constipation in patients with hard stool or specific conditions & for people who should avoid straining .**

Fecal Softeners (Lubricants)/surfactants



Drugs

- **Docusate**
- **Glycerin**
- **Paraffin oil**



Docusate

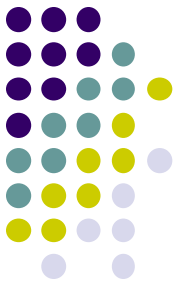
- **Sodium dioctyl sulfosuccinate**
- **One type of surfactants**
- **Act by decreasing surface tension of feces**
- **is given orally (12-72 hours) or enema (5-20 min).**

Paraffin oil

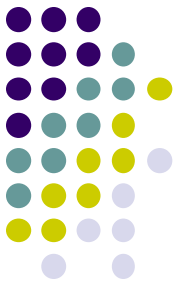
- **Is a mineral oil, given orally**
- **acts as lubricant thus softening the feces & promoting defecation**
- **Good for radiology preparation**
- **not palatable**
- **impairs absorption of fat soluble vitamins.**

Glycerin

- **Lubricant**
- **Given rectally (suppository).**

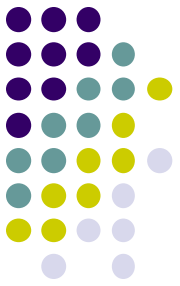


Irritable bowel syndrome (IBS)



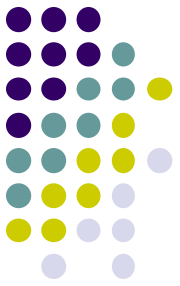
Chronic bowel disorder characterized by abdominal discomfort (bloating, pain, distention, cramps) associated with alteration in bowel habits (diarrhea or constipation or both).

Symptomatic treatment of IBS

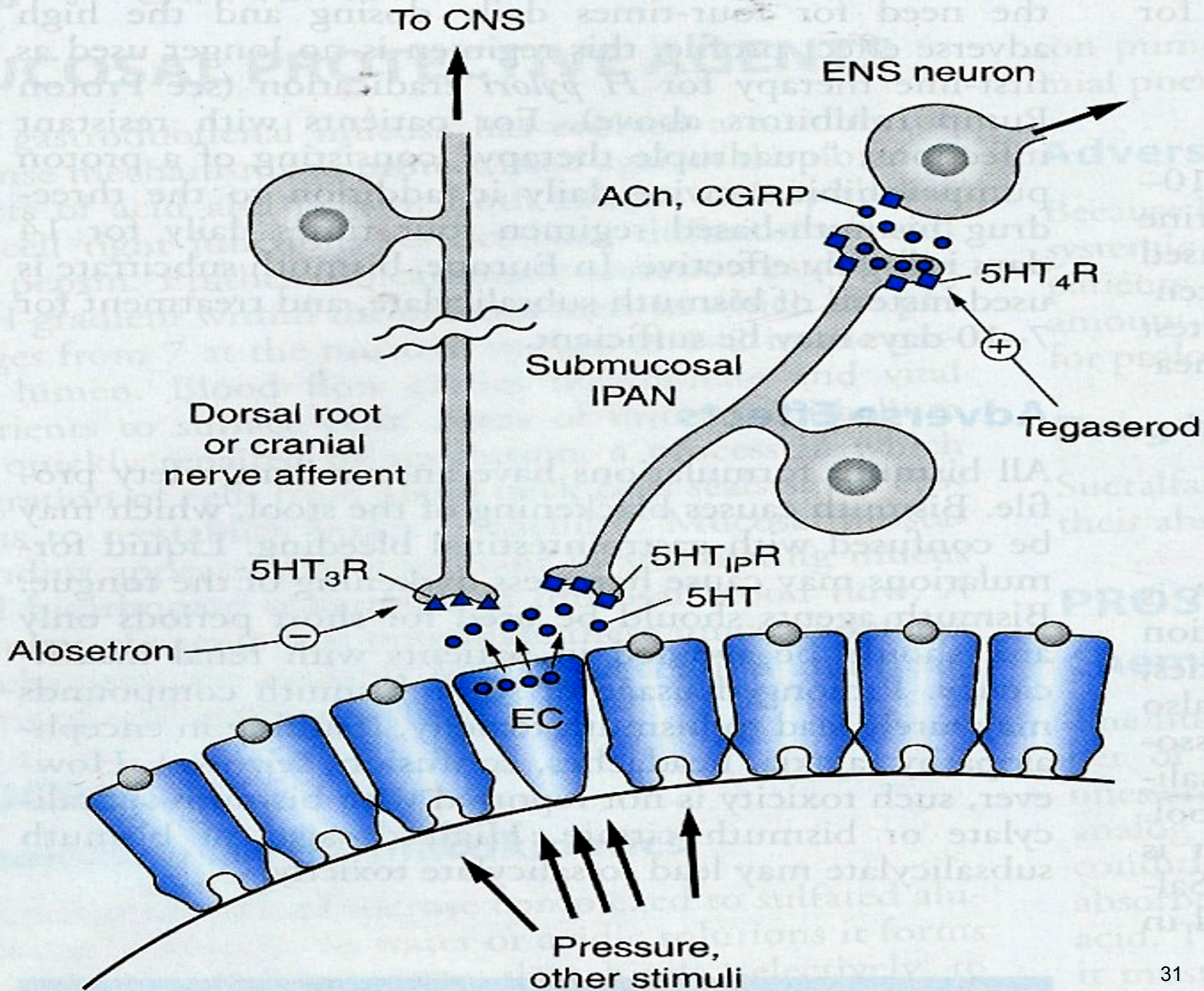


- **Antispasmodics e.g. mebeverine**
- **Low doses of tricyclic antidepressants (amitriptyline) act via**
 - **Anticholinergic action**
 - **Reduce visceral afferent sensation**
- **Laxatives in IBS with Constipation**
- **Antidiarrheals in IBS with diarrhea (diphenoxylate – loperamide).**
- **Alosetron (IBS-D)**
- **Tegaserod (IBS-C)**

Alosetron



- **Selective 5HT₃ antagonist**
- **5-HT₃ receptors antagonism of the enteric nervous system of the gastrointestinal tract results into:**
 - **inhibition of colon motility**
 - **inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating).**



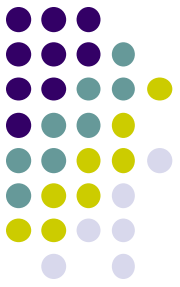
Uses of Alosetron

Used in IBS with severe diarrhea in women who have not had success with any other treatment.

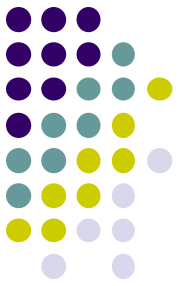
Adverse effects

Constipation & ischemic colitis may occur.

People taking alosetron must sign a consent form before starting to take the medicine.



Tegaserod



- 5HT₄ agonist
- Stimulation of 5HT₄ of enteric nervous system of GIT → increases peristalsis
- Short term treatment of IBS-associated with constipation in women <55 years old with no history of heart problems
- Tegaserod has CVS side effects
- may still be used in limited emergency situations.

Summary



Bulking agents	Oral, 48–72 hours	Acute & chronic constipation
stool softeners	oral, 24–72 hours; rectal, 5 --20 minutes	prevention of straining after rectal surgery and in acute perianal disease
Osmotic laxatives (lactulose)	oral, 24–72 hours	- chronic constipation -hepatic encephalopathy - opioid constipation
Saline laxatives	oral, 0.5–3 hours; rectal, 30 minutes	short term treatment of moderate-to-severe constipation; acute constipation; bowel preparation for colonoscopy