

Drugs Used for Constipation



Eman Alrashidi , Bedoor Alqadrah , Sarah Bin Husain , Shoog Alageel

Ibrahim Alshiddi , Sultan Alsalem , Ismail Raslan

- > Team notes are in **purple**.
- > Important points are in **red**.

Constipation

Definition:

Too infrequent passage of stool that may be due to decreased motility in colon or due to difficulty in evacuation.

Causes: see Table

1. Diet : Decrease in water and fiber contents of diet.
2. Local Painful Conditions : Anal fissures, Hemorrhoids.
3. Lack of muscular exercise.
4. Drugs: Muscle relaxants, Anticholinergics (e.g. Atropin), Calcium channel blockers , analgiscs drug (e.g. morphine)

However, Doctors (some times) may consider a source of chronic constipation. How?

*** Chronic use of stimulant laxatives causes nerve damage which will lead to chronic constipation.**

TABLE 1. Common Causes of Constipation

Drugs Analgesics Antacids Anticholinergics Antidepressive agents Anti-Parkinsonism agents Barium sulfate Bismuth Diuretics Iron sulfate Opiates	Neurogenic Cauda equina tumor Cerebrovascular accidents Chagas' disease Hirschsprung's disease Multiple sclerosis Parkinson's disease Shy-Drager syndrome Tumors
Large Bowel Diseases Anal fissure Anal stenosis Chronic volvulus Dermatomyositis Diverticular disease Irritable bowel syndrome Rectal prolapse Scleroderma Strictures Endometriosis Ischemic colitis Lymphogranuloma venereum Surgery Tumor	Metabolic and Endocrine Amyloid Diabetic neuropathy Hypothyroidism Hypercalcemia Hypokalemia Porphyria Pregnancy Uremia Diet Inadequate fiber intake Inadequate fluid intake

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 laxatives.



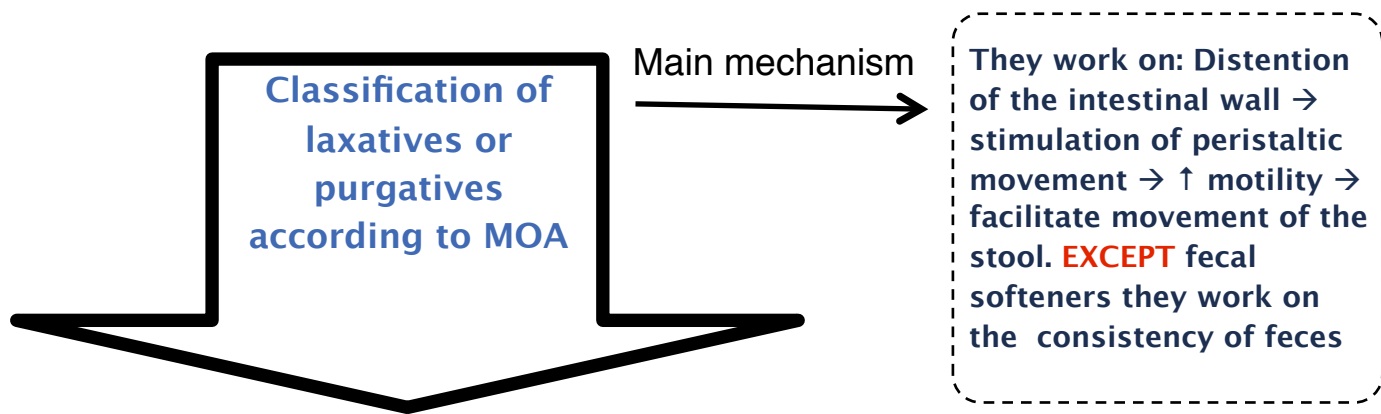
Term of strong
laxatives

●Drugs (laxatives = purgatives= cathartics):

Drugs that hasten the transit of food through the intestine by several methods .

●Classification of laxatives based on MOA

1. Bulk Purgatives : Increase volume of nonabsorbable solid residue (fiber).
2. Osmotic Purgatives (salts or sugars): Increase water content in large intestine.
3. Stimulant (or irritant) Purgatives :Increase motility and secretion (by stimulating ENS).
4. Fecal softeners (lubricants): Alter the consistency of feces → easier to pass.



Bulk Purgatives : Increase volume of nonabsorbable solid residue

- Dietary fibers
- Natural plant products & semi synthetic hydrophilic colloids (e.g : Psyllium seed, methyl cellulose & Carboxymethyl cellulose (CMC)) .
- Synthetic non absorbed resins (e.g :Calcium polycarbophil (

Osmotic Purgatives : Increase water content in large intestine.

- Organic -Sugars- : Lactulose
- Non-organic -Saline purgatives- (e.g : Magnesium sulphate , Magnesium hydroxide , Sodium phosphate or potassium phosphate)

Stimulant Purgatives : Increase motility and secretion.

- Bisacodyl
- Anthraquinone derivatives (e.g : (senna, cascara, aloes (الصبار))
- Castor oil (زيت خروع)

Fecal softeners (lubricants) : Alter the consistency of feces → easier to pass.

- Surfactants (e.g. Docusate (
- Glycerin (Suppository)
- Mineral oil (Liquid Paraffin)

1st) Bulk Purgatives

Most important and commonly used

- **MOA:** – **Non absorbed** hydrophilic colloids* → Increase the bulk of intestinal contents by water absorption (retention) → ↑ mechanical pressure on the walls of intestine → stimulation of stretch receptors → ↑ peristalsis.

Note: 1 gm of Carrot absorbs 20 gm of water.

* colloids : substance have high molecular weight , can not be absorbed & have ability to absorb water

• Members

1. Dietary fibers (natural): undigested polysaccharide vegetables, fruits, grains, bran **نخالة أو بر** , pectin.
2. Natural plant products & semi synthetic hydrophilic colloids (very important)
Psyllium seed, methyl cellulose
Carboxymethyl cellulose (CMC).
3. Synthetic non absorbed resins
Calcium polycarbophil.

• Side Effects (or disadvantages)

1. **Delayed onset of action** (1–3 days).
>> so not used in acute cases
2. Intestinal obstruction (should be taken with enough water).
[without water causes obstruction]
3. Malabsorption syndrome, abdominal distention.
4. Interfere with other drug absorption e.g. iron, calcium, and cardiac glycosides.

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Constipation

• Clinical Uses

1. Hemorrhoids
2. Anal fissure
3. Pregnancy
4. Colostomy & ileostomy
5. Inflammatory Bowel Disease (Ulcerative Colitis)
6. Chronic diarrhea associated with diverticular disease.

2nd) Osmotic Purgatives

- **MOA:** – **Soluble** but non absorbable compounds
 - Increase water content in large intestine.
 - They remain in the bowel and retain water by osmosis thereby increasing the volume of feces → ↑ distension → ↑ peristalsis → evacuation of watery stool.

• Members

- a) Organic (Sugars) : Lactulose (semisynthetic disaccharide of fructose and galactose).
- b) Non-organic (Saline purgatives) :
Magnesium sulphate or hydroxide
Sodium or potassium phosphate.

a)organic: **Lactulose:**

- **MOA:** – Non absorbable disaccharide .
 - Metabolized by colonic bacteria into fructose and galactose
 - These sugars (**fructose+galactose**) are fermented into lactic acid and acetic acid that function as osmotic laxatives (**retain water inside GIT**).

- **Uses:**

1. Prevention of chronic constipation
2. **Treatment of liver cirrhosis & hepatic encephalopathy** * (1st choice)
Lactulose favors the formation of the nonabsorbable NH_4^+ from NH_3 , trapping NH_3 in the colon and reducing plasma NH_3 concentrations.

* Why Lactulose is commonly used in liver cirrhosis?

First : What happen in liver cirrhosis ?

ammonia is normally absorbed by intestine & go to the liver to be removed . in Patients with liver cirrhosis , liver can't remove ammonia → accumulation of ammonia (toxic) in the blood → hepatic encephalopathy

!! Because of that, patients with liver cirrhosis are also recommended to reduce the amount of meat intake to reduce accumulation of ammonia

Second : What is the mechanism of lactulose in treatment ?

Lactulose --> Lactic acid + Acetic Acid → acidification of the colon →
↓ ammonia absorption → ↑ excretion of ammonia in feces.

Side Effects

- * **Delayed onset of action** (2–3 days)
- * Abdominal cramps and flatulence.
- * Electrolyte disturbance (but less than saline).

- Dose: 15 ml for constipation and 30 ml for liver cirrhosis

b)Non-organic: Saline Purgatives:

- **MOA:** –Are poorly absorbed salts.
 - They remain in the bowel and retain water by osmosis thereby increasing the volume of feces → ↑distention → ↑peristalsis → evacuation of watery stool.
 - **Rapid effect** (within 1–3h). [acute cases because they are very effective]
 - Isotonic or hypotonic solution should be used.
(hypertonic lead to severe dehydration “should be avoided”)

•Members:

1. Magnesium sulphate (Epson’s salt).
2. Magnesium hydroxide (milk of magnesia).
3. Sodium phosphate or potassium phosphate.

•Uses (in minor condition because of their side effect)

1. Treatment of acute constipation
2. Prevention of chronic constipation
 - * *What other uses for magnesium sulphate?*

Arrhythmias & eclampsic convulsions

•Side Effects

1. Intravascular volume depletion. (used in the past to treat hypertension)
2. Electrolyte fluctuations (Disturbance of fluid and electrolyte balance): severe in children.
3. May have Systemic effect (depend on the dose)

* However, all these side effects have no clinical importance because little amount of Mg will be absorbed AND it’s used only for short times to treat acute cases.

• Contraindications !!

1. Elderly patients
2. Renal insufficiency. (Cause hypermagnesemia)
3. Sodium salts in CHF (cardiac patient).
4. Magnesium salts in renal failure, heart block, CNS depression, neuromuscular block.

Not important!

Balanced polyethylene glycol (PEG)

- Balanced isotonic solution of osmotically active sugar, NaCl, KCl, Na , HCO₃
- No intravascular fluids or electrolyte shifts
- No flatus or cramps
- Lavage solution
- **Mainly** Used for complete cleansing prior to gastrointestinal endoscopic procedures (4L over 2–4 hours).
- Small doses used for treatment or prevention of chronic constipation.

3rd) Stimulant Purgatives (cathartics)

• MOA:

-act via direct stimulation of enteric nervous system (ENS)→ peristalsis &purgation.

• Side Effects

5. Abdominal cramps may occur.
6. Prolonged use → **dependence & destruction of myenteric plexus and atonic colon.** → **chronic constipation**

• Contraindications !!

4. in lactation.
5. Castor oil in pregnancy → reflex contraction of uterus → abortion

• Members:

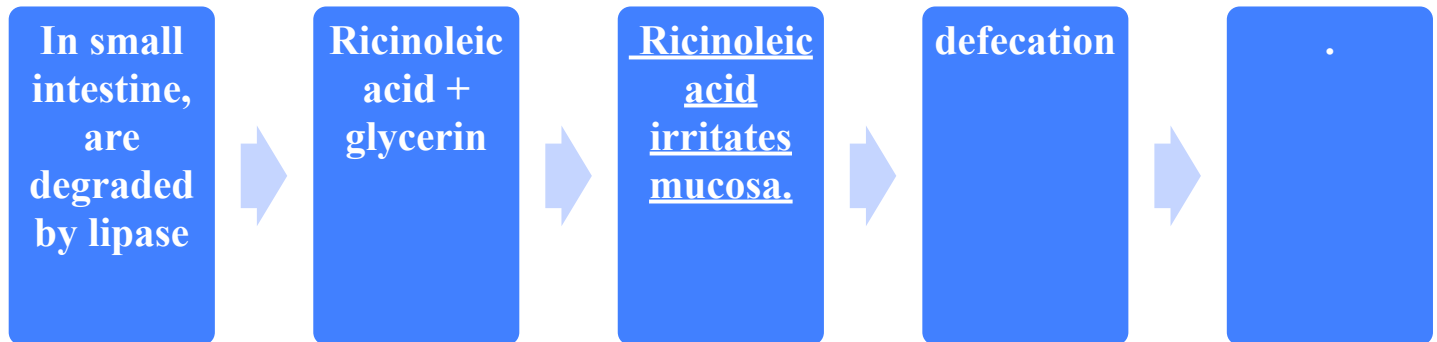
- a-Bisacodyl.
- b-Castor oil. **زيت خروع**
- c- Anthraquinone derivatives.

a) **Bisacodyl (Dulcolax®)**

- Acts on large intestine (weak).
- Onset time 6–10 h, taken at night.

b) **Castor Oil** (its action by ricinoleic acid)

- **MOA:**

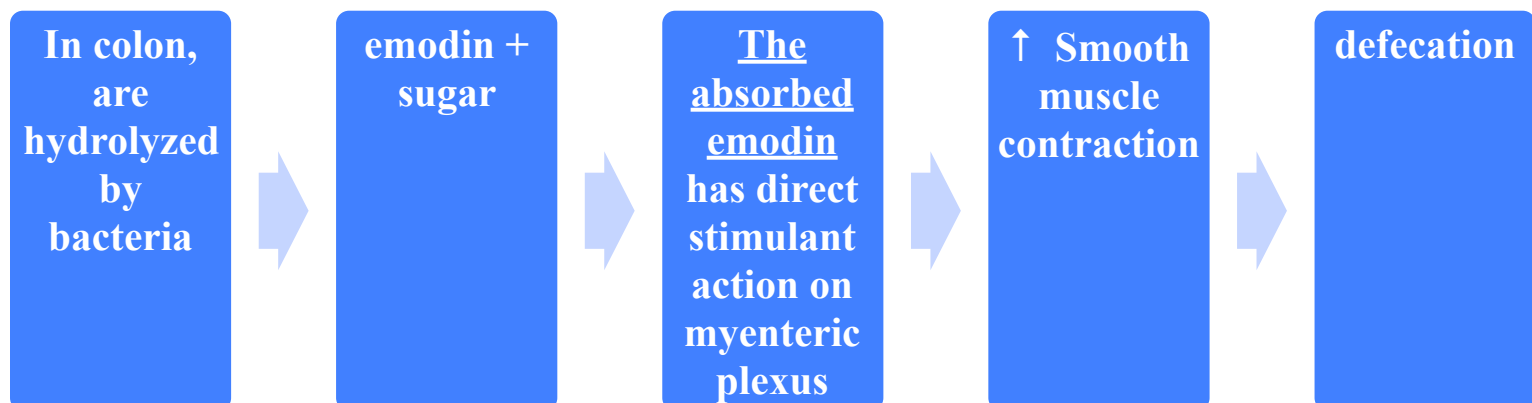


- Acts on small intestine (strong).
- 5–20 ml on empty stomach in the morning.
- onset time = 4 h.

c) **Anthraquinone derivatives**

- Senna, Cascara, Aloes صبار

- **MOA:**



- Bowel movements in 12 h (orally) or 2 h (rectally).
- Given at night.
- Can cause Brown pigmentation of the colon (melanosis coli).
- Emodin may pass into milk.

Common stimulant purgatives			
Drugs	Type	Site of Action	Onset of Action
Cascara	Anthraquinone	colon	6-8 hours
Senna	Anthraquinone	colon	6-8 hours
Aloe vera	Anthraquinone	colon	8-10 hours
Bisacodyl	Diphenylmethane	colon	6-12 hours
Castor Oil	ricinoleic acid	small intestine	2-6 hours

4th) Fecal Softeners (Lubricants)

- **MOA:** –Are non absorbed drugs that soften the feces thus promoting defecation.

– decrease surface tension lead to increase diffusion of water into stool thus will lead to softness of stool.

- May be given orally or rectally.

• Members :

1. Surfactants

- decrease surface tension of feces
- e.g. **Docusate** (sodium dioctyl sulfosuccinate).
is given orally or enema (injection of liquid into the rectum through the anus)
- Used to treat constipation in patients with hard stool and for people who should avoid straining (e.g Hemorrhoid & hospitalized patients – especially after surgery-)

2. **Glycerin** (Suppository= تحاميل). [given after prostate or hemorrhoids surgery also given to children]

3. Mineral oil (**Liquid Paraffin**).

[given to patients in preparation of procedures that require clear colon]

Side effects of liquid paraffin

Not palatable (bad taste)

impairs absorption of fat soluble vitamins.

Increase activity of oral anticoagulant.

Purgatives	Site of action	Onset time
Bulk purgatives	Small & large intestine	12-72 h
Saline purgatives	Small & large intestine	1-3 h
Lactulose	colon	12-72 h
Mineral oil	colon	6 – 8 hours
Docusate	Small and large intestine	12 – 72 hours
Stimulants	Small intestine Colon	Castor oil Bisacodyl anthraquinones