CONSTIPATION

Pharmacotheraphy of Constipation (Laxatives)

What is constipation?

- Constipation is generally defined as infrequent and/or unsatisfactory defecation fewer than 3 times per week.
- Patients may define constipation as passing hard stools or straining, incomplete or painful defecation.

Constipation is a symptom, NOT a disease.

Classification of laxatives (according to the mechanism of action)

Bulk purgatives

- Dietary fiber----Bran, methylcellulose, ispaghaula

Stool softeners

- Docusates, liquid paraffin.

Stimulant or irritant purgatives

- , Bisacodyl.
- senna, Cascara sargada.

Osmotic /saline purgatives

magnesium sulphate, magnesium hydroxide, sodium phosphate, sodium sulphate,

Sodium potassium tartarate, lactulose.

Prokinetic agents

- *5-HT_4 agonist*---- Tegaserod

Chloride channel activators.

- lubiprostone

Laxatives Classification

Bulk laxatives	• Agar fibers, methyl cellulose and bran
Osmotic laxatives	• Magnesium hydroxide, and lactulose
Stimulants or irritant	• Castor oil and Bisacodyl
Stool softeners	Dioctyl, Liquid paraffin and Glycerin suppository

Bulk purgatives

- They are indigestible , hydrophilic substances (colloids) that absorb water in the large intestine forming gels . These gels due to absorption of large amount of water cause water retention and increase the bulk of the stools . They exert mechanical distension on the large bowel , promote peristalsis and ultimately defaecation.
- Large amount of fluids should be taken along with them to avoid intestinal obstruction.
- **CONTRAINDICATIONS**
- Should be avoided in those with mega colon and those who are immobile to avoid intestinal obstruction.
- **SIDE EFFECTS;** abdominal discomfort, distension/fullness
- *Methylcellulose , psylium seeds* and bran all exert their effect via this mechanism of action.

Stool softeners

- Emollient laxatives and surfactants are stool softeners. (acts in 1---3 days)
- **Docusates:** they are anionic detergents. That is they are lipophilic and hydrophilic.
- They reduce the surface tension of the stools. Thus enabling the stools to allow the accumulation of fluid and fatty substances , making the stools soft.
- **Mineral oils (liquid paraffin):** it is a mineral oil so taken orally.
- They reduce the surface tension of the stools , penetrate , soften the stools .
- Liquid paraffin has a lubricant effect and ease the passage of stools.
- It is a preferred laxative in cardiac patients as the patient doesn't need to strain.
- **Adverse effects of liquid paraffin:**
- May pass into lungs while taking it orally leading to **lipid pneumonia.** Also regurged into lungs, so better avoided at bed time.
- Long term use may lead to malabsorption of fat soluble vitamins A, D,E, K.
- As the stools are oily so they may leak through the anal sphincter and soil the clothes

Stimulant / irritant purgatives

- These directly act on the enteric neurons and the gastric mucosa.
- They enhance the PG c AMP in the gastric mucosa.
- They inhibit Na^{+}, K^{+}- ATPase activity in the GIT.
- The net effect of which is increased secretion of electrolytes by the mucosa and thus induce peristalsis.

Senna and Cascara

- It is widely used as stimulant laxative. Its active ingredient is a group of sennosoides, a natural complex of anthraquinone glycosides.
- Administered orally.
- They are poorly absorbed from the small intestine. The unabsorbed part reaches the large intestine and reduced to ***anthrol*** by the local bacteria.
- Anthrol induces purgation . Causes secretion of water and electrolytes.
- Evacuation occurs in 8—10 hours of intake.
- In combination with docusate it is used to treat opioid induced constipation.
- **Side effects**
- are dependence, skin rashes, black pigmentation of the colonic mucosa and brownish discoloration of urine.
- **Contraindications;**
- Pregnancy, lactating mother.

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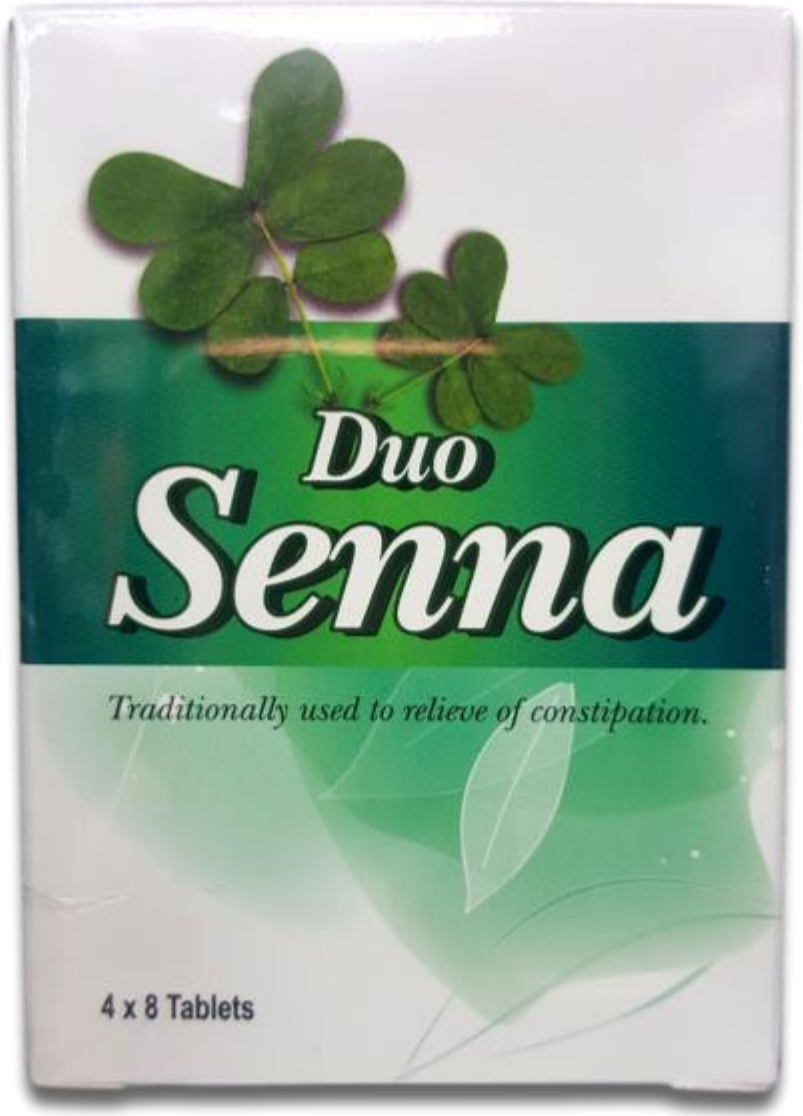
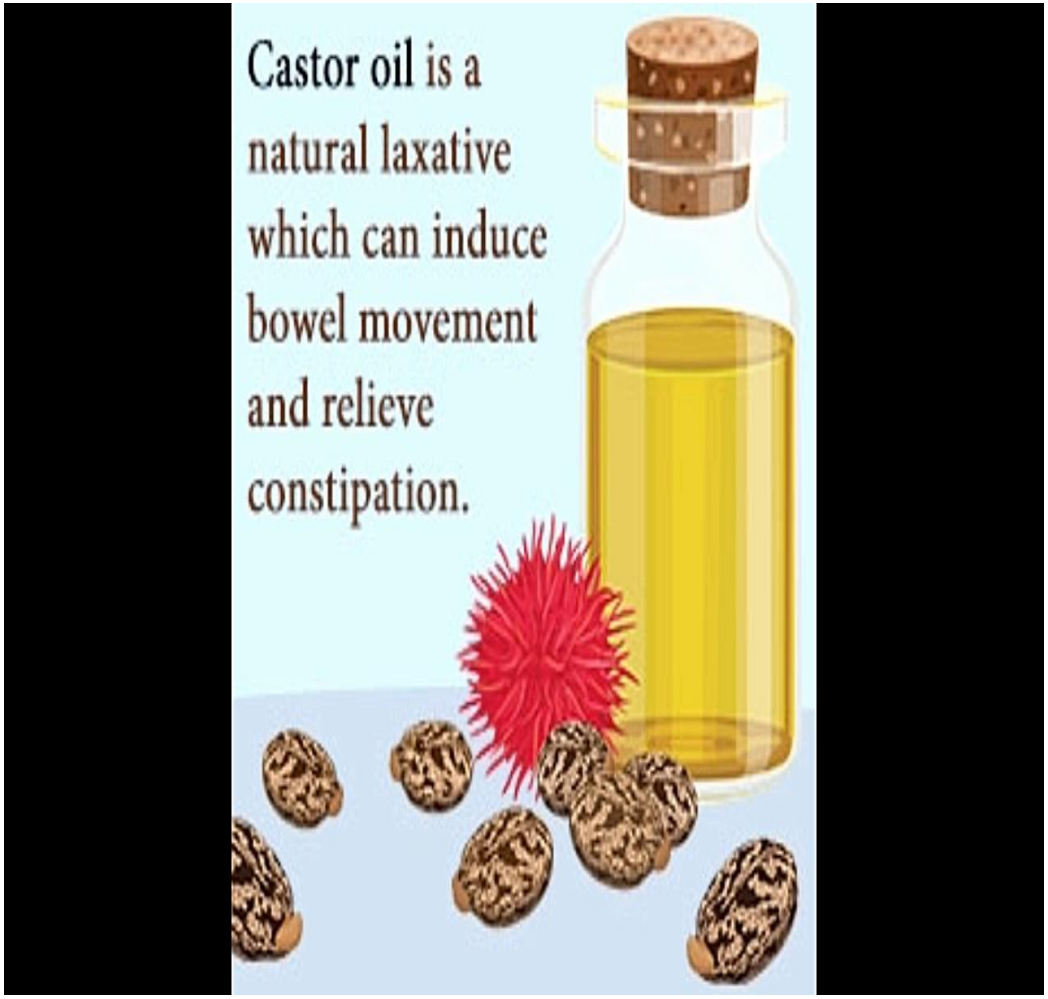
- **Bisacodyl:**
- It acts directly on the nerve fibers in gastric mucosa of the colon
- They available as .suppositories and enteric coated tablets .
- It is poorly absorbed after oral intake
- It undergoes activation by esteases in the bowel.
- After oral intake the effect is seen after 6—8hrs.
- That is why it is given at bed time so that the bowel gets evacuated early in the morning. Rectal suppositories cause evacuation in 1-2 hours.
- used prior to endoscopy , surgery or radiological investigations.
- Should not be taken along with the drugs that elevate pH.
- Should not be taken with milk as it also elevates pH.
- **Side effects;**
- Elevated pH may result in early disruption of enteric coating and cause severe stomach irritation.
- Prolonged use may lead to atonic colon.


OVERNIGHT
RELIEF
Dulcolax
Pink
LAXATIVE TABLETS
(bisacodyl USP 5mg)
Gentle Enough For
Sensitive Stomachs
#1
COMFORT COATED
TABLETS


Fleet
stimulant laxative
BISACODYL
enema
ready-to-use
soft, flexible
Comfortip®
latex-free
#1 DOCTOR
RECOMMENDED


Duo
Senna
Traditionally used to relieve of constipation.
4 x 8 Tablets

- **Castor oil:**
- When taken , it is broken down in the small intestine to recinoleic acid.
- It is very irritating to the stomach and induce strong peristalsis leading to evacuation of bowel.
- It should be avoided in pregnant women as it may also lead to uterine contractions.


Castor oil is a
natural laxative
which can induce
bowel movement
and relieve
constipation.

Osmotic / saline purgatives

- They are the most powerful purgatives
- They act very rapidly
- Magnesium, potassium and sodium salts are included in this group.
- They persist in the lumen and exert osmotic effect.
- Magnesium also release cholecystokinins. They draw water into the lumen, thereby distending the lumen and thus induce peristalsis.

- There taste is vey bitter so often fruit juices are added to it.

- ***Magnesium sulphate:(epsom salt)***
- On oral administration they induce purgation. When given parentally induce uterine relaxation , CNS depression and cardiac depression.
- ***Magnesium hydroxide:(milk of magnesia)***
- Used as an antacids.
- Should be avoided in children and those compromised renal functions as they cause CNS and cardiac depression.

osmotic purgatives, given orally in the morning

↓

act on the small and large intestine

↓

not absorbed in the gut

↓

draw fluid by osmotic activity into the gut.

Mg^{2+} release colecystokinins

↓

cause abdominal distention

↓

stimulate peristalsis

↓

evacuation of watery stools in 1—3 hours

Lactulose

- It is a disaccharide of fructose and galactose.
- Commonly used in those with hepatic coma and also reduce blood ammonia level.
- Orally not absorbed from GIT.
- Acted upon by the colonic bacteria which convert it into short chain fatty acid . This short chain fatty acid exerts osmotic pressure and induce peristalsis.
- they draw water and electrolytes into the lumen and also reduce the pH
- This favors the conversion of ammonia into polar ammonia ion. This ammonium ion is non absorbable . Hence blood ammonia level is reduced.
- Lactulose should be taken with plenty of water to soften the stools and also induce purgation.
- **Indication;**
- Constipation
- Hepatic encephalopathy
- **Side effects**
- Abdominal discomfort,cramps,
- Flatulence.


Duphalac
(Lactulose
Syrup)
66.7g/100ml
240 ml

Lactulose

Colonic bacteria

Short chain fatty acids

Reduce luminal Ph In the colon → **ammonia** → **ammonia ions** → Blood ammonia level drops

ammonia → Unabsorbed in gut

Chloride channel activator

- Lubiprostone is the only drug belonging to this class of drugs.
- It acts by stimulating the chloride channels to increase the fluid secretion into lumen of the intestines.
- This eases the passage of stools with negligible changes in the electrolyte balance. Also no tolerance have been seen with it neither any drug –drug interactions have been observed with the use of lubiprostone.

Uses of laxatives with preparation of choice

- Acute functional constipation --- bulk laxatives.
- To avoid straining during defeacation in cardiovascular patients, those who had eye surgery, hernioraphy- etc-----docusates are given
- In hepatic coma ----lactulose is given
- Preoperatively ,colonoscopy------ bisacodyl is given
- Following anthelmentic therapy ------ osmotic purgatives are given
- In drug poisoning ----------osmotic purgatives are recommended.


The
End