بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pharmacology | FINAL 3

Laxative & Anti-diarrheal drugs

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Laxatives

Osmotic Laxatives(Purgatives):

- Soluble nonabsorbable compounds that result in increased stool liquidity due to an obligate increase in fecal fluid.
- **Magnesium oxide (Milk of Magnesia):** (ملح إنجليزي)
  - Can cause hypermagnesemia.
  - Large doses of magnesium citrate and sodium phosphate can cause Purgation: rapid bowel evacuation within1-3 hours. This might cause volume depletion.

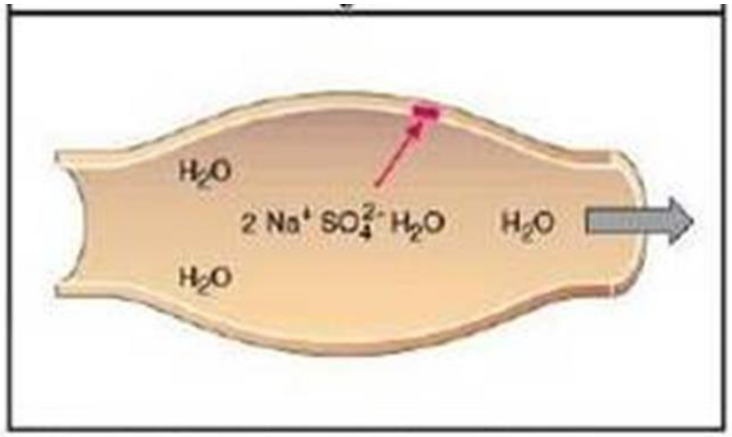
لما حط أبو غالب ملح إنجليزي بالخبز لأبو بشير:(

Laxatives

Generally, the osmotic laxatives can be used as an alternative for the previously mentioned laxatives.

Osmotic Laxatives:

- **Sorbitol.**
- **Lactulose:**
  - **Sugars metabolized by bacteria producing severe flatus and cramps** as side effects **.**



C. Osmotically active laxatives

Extra explanation :-

- The difference between bulk-forming laxatives and osmotic laxatives is that bulk-forming laxatives work by absorbing water and increasing stool bulk, which distends the colonic wall and stimulates peristalsis. In contrast, osmotic laxatives work by drawing water into the intestinal lumen, increasing stool liquidity and facilitating bowel evacuation.

- The difference between sorbitol/lactulose and magnesium oxide is that sorbitol and lactulose are metabolized by colonic microbiota, producing gases that can cause bloating, flatulence, and abdominal cramping, whereas magnesium oxide mainly acts by osmotically retaining water in the intestinal lumen.

Extra information by Abdalrhman Froukh:-

- Lactulose has an extra function besides its role as an osmotic laxative. It is commonly used in hepatic encephalopathy. Lactulose is metabolized by the normal colonic flora into lactic acid and acetic acid, which lower the colonic pH. The acidic environment converts ammonia (NH_3) into ammonium (NH_4^+), a charged form that cannot be easily absorbed through the intestinal wall. As a result, ammonia becomes trapped in the colon and is excreted in the stool instead of entering the circulation and reaching the brain.

- **((YOU CAN DELETE THIS SLIDE))**

Laxatives

Osmotic Laxatives:

- **Balanced Polyethylene Glycol:**

(alternative for the previously mentioned osmotic laxatives)

- **Safe solution: NO intrvascular fluid or electrolyte shifts.**
- **Does Not cause cramps or flatus.** (but sorbitol does)
- **Used for complete colonic cleansing before endoscopy.**
- **PEG is an inert, non-absorbable, osmotically active sugar.**
- **Sodium sulfate, chloride, bicarbonate and potassium chloride**(explained in the next slide)
- **For colonic cleansing—> it should be ingested rapidly (4L over 2-4hs).**
- **For chronic constipation**(Continuously used) **,PEG powder is mixed with water or juice .**

Sodium sulfate, chloride, bicarbonate and potassium chloride

Extra Explanation:

- This electrolytes are added because **PEG alone** draws large amounts of water into the intestine, which may cause dehydration and electrolyte imbalance.

- Sodium and potassium salts help maintain electrolyte balance during bowel cleansing.

- PEG + added electrolytes = **Balanced GEG** which is very safe solution without intravascular fluid or electrolytes shift.

Laxatives

Stimulant Laxatives(Cathartics):

Mechanism Of Action:-

- **Direct stimulation of the enteric system.**

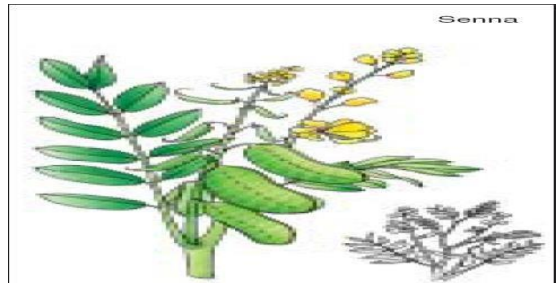
RESULTS IN:-

- **Colonic electrolyte and fluid secretion.**
- **Can lead to dependence and destruction of the myenteric plexus** because of continuous stimulation of the ENS **resulting in colonic atony and dilation.**
- **May be needed in neurologically impaired patients and in bed- bound patients in long term care facilities.**
  (not normal patients)

Laxatives

- **Stimulant Laxatives(Cathartics):**

Naturally based products



- **Anthraquinone Derivatives:**
  - **Aloe.**
  - **Senna.**
  - **Cascara.**
    - **Poorly absorbed .**
    - **After being hydrolysed , produce bowel movement that** stimulate bowel emptying **in (<u>6-12</u>) hours.**
    - **Cause brown pigmentation of the colon <u>"Melanosis Coli".</u>**
    - **Not carcinogenic.**

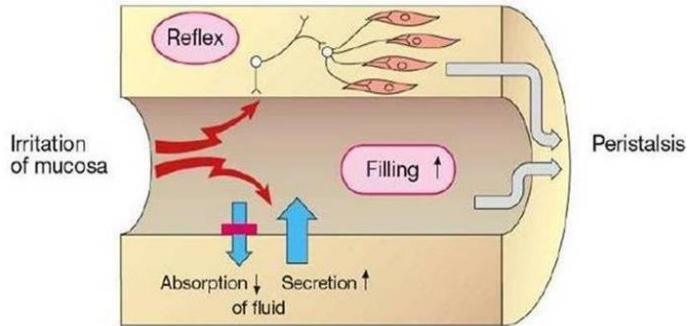
The safe thing about them is they're **<u>natural products</u>** originally.

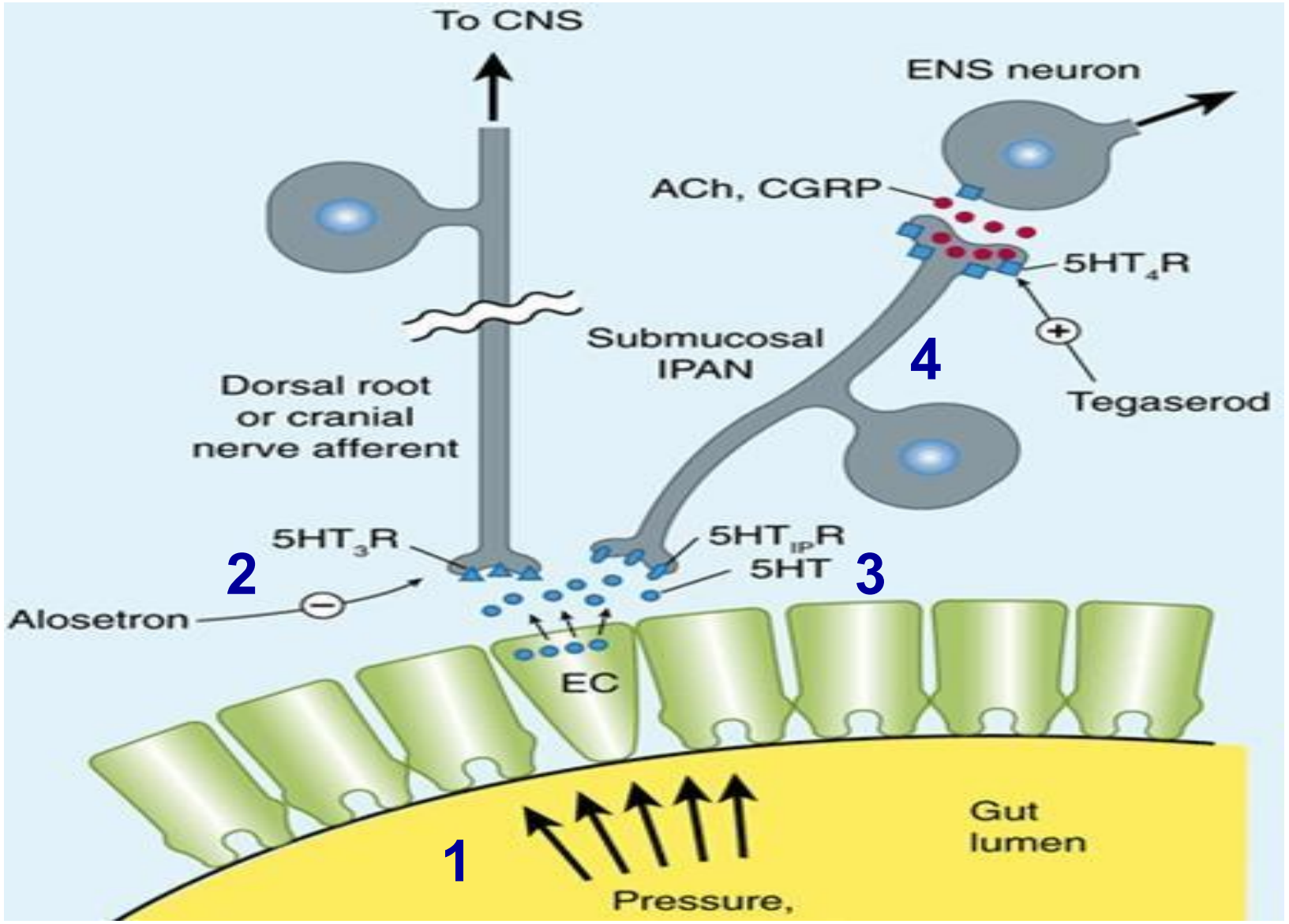
Laxatives

- **Stimulant Laxatives(Cathartics):**
- **Castor Oil:**

It's a laxative that's used to clean the colon before procedures.

- **Hydrolyzed in upper intestine into ricinoleic acid which is a <u>local irritant.</u>** That results in stimulation of the emptying of colon content.
- **Was used as purgative to clean the colon before procedures.**





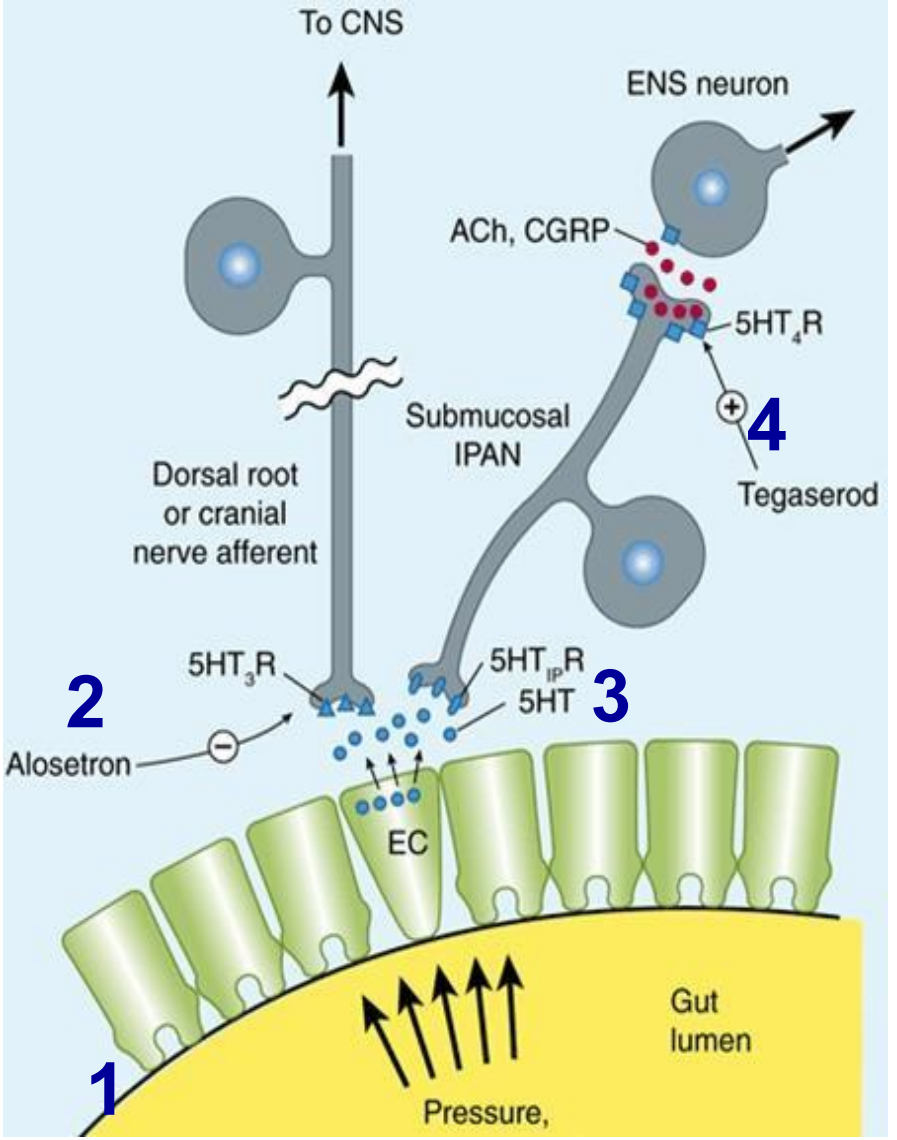
Mechanisms that stimulant laxatives mimic to enhance bowel motility.

Normal situation

1-Gut distention(after eating and filling of the stomach) stimulates 5-HT release from EC cells.
(5 hydroxytryptamine=5-HT= serotonin)

2-Stimulation of **5-HT3R** receptors on the **extrinsic afferent nerves** (sensory nerves) ; stimulate **nausea, vomiting**, or **abdominal pain**.

3- 5-HT also stimulates **5-HT1P** receptors of the **intrinsic primary afferent nerves (IPANs)** which activate the enteric neurons responsible for **peristaltic and secretory reflex activity.**



4- Stimulation of 5-HT4 receptors (5-HT4R) on presynaptic terminals of IPANs enhances release of **ACh** & calcitonin gene related peptide (**CGRP**), promoting reflex activity

Laxatives

Tegaseroid:

- Is a serotonin 5-HT_4 partial agonist, which are presynaptic receptors of the submucosal intrinsic primary afferent nerves which enhance the release of their neurotransmitters.
- These neurones stimulate proximal bowel contraction(via ACh and substance P) and distal relaxation(via nitric oxide and VIP).
- The drug promotes gastric emptying and small and large bowel transit but has no effect on esophageal motility.
- Also stimulates cAMP-dependent chloride secretion leading to increased stool liquidity.

Laxatives

Tegaseroid:

Clinical Uses:

- **Chronic constipation. Nonulcer dyspepsia.**
- **Gastroparesis.**
- **Irritable bowel syndrome.**

Adverse Effects:

- **Extremely safe drug.**
- **Diarrhea occurs in 9% ofpatients but resolves within days.**
- **Expensive.**

Key summary for quick revision :)

LAXATIVES

Drugs that promote bowel movements by increasing stool **bulk**, **water content**, or **intestinal motility**.

Used for constipation
Also used for bowel cleansing before endoscopy or surgery

TYPE	MECHANISM OF ACTION	EXAMPLES	KEY POINTS / USES	ADVERSE EFFECTS / NOTES
1. BULK-FORMING LAXATIVES  (Fiber)	• Non-absorbable fibers absorb water. • Increase stool bulk → distend colon → promote peristalsis. 	• Psyllium (ispaghula) • Methylcellulose • Calcium polycarbophil	• **First-line** for chronic constipation. • **Onset:** 12–72 h • Take with plenty of **water**. • Natural option.	• Bloating, flatulence • May cause obstruction if taken without water. • Not suitable in bowel obstruction.
2. OSMOTIC LAXATIVES 	• Retain water in intestinal lumen by osmotic effect. • Increase stool liquidity → facilitate bowel movement. 	**Non-absorbable sugars:** • Lactulose • Sorbitol	• Useful for chronic constipation. • **Lactulose:** also used in **hepatic encephalopathy**.	• Bloating, cramping, flatulence (more with lactulose, sorbitol).
		Saline laxatives: • Magnesium salts (e.g., $Mg(OH)_2$, $MgSO_4$) • Sodium phosphate	• **Saline laxatives:** act quickly.	• Electrolyte imbalance possible (with excessive or long-term use of saline laxatives).
		PEG (Balanced electrolyte solution)	• **PEG (Polyethylene Glycol):** – Iso-osmotic, non-absorbable. – Safe: no significant fluid or electrolyte shifts. – Does not cause cramps or flatulence like sorbitol. – Used for complete colonic cleansing before endoscopy. – Should be ingested rapidly (4 L over 2–4 h). – For chronic constipation: PEG powder mixed with water/juice.	• **PEG** is safest; minimal electrolyte or intravascular fluid shifts. • Added electrolytes (Na^+, K^+, Cl^-, HCO_3^-, SO_4^{2-}) prevent imbalance and dehydration.
3. STIMULANT (CATHARTIC) LAXATIVES 	• Direct stimulation of enteric nervous system (ENS). • ↑ Peristalsis and ↑ fluid secretion → rapid bowel movement. 	• Senna • Aloe • Cascara • Castor oil	• Used short-term for constipation. • **Senna:** natural product. • **Castor oil** → converted to ricinoleic acid (local irritant) → strong stimulation.	• Abdominal cramping, diarrhea • **Melanosis coli** with senna (brown pigmentation, not carcinogenic). • Chronic use → damage to **myenteric plexus** → colon atony, dilation, **dependence**. • **Avoid long-term use** in normal individuals (except in bedridden or neurologic impairment).
4. STOOL SOFTENERS (EMOLLIENTS) 	• Increase water and fat penetration into stool. • **Soften** stool → easier evacuation.	• Docusate sodium • Docusate calcium	• Useful for mild constipation. • Often used with stimulant laxatives. • Safe for long-term use.	• Minimal side effects. • May cause mild GI upset.

PHYSIOLOGIC MEDIATOR

Hydroxytryptamine (Serotonin, 5-HT) 

- Released from **enterochromaffin (EC) cells** in GIT in response to distension, food, or irritation.
- Stimulates ENS → ↑ motility, ↑ secretion.

Receptors:

- **5-HT_4:** ↑ peristalsis & secretion (pro-motility effect)
- **5-HT_3 (on extrinsic afferent nerves):** stimulation → **nausea**, **vomiting**, abdominal pain. (Target of 5-HT_3 antagonists e.g., **ondansetron**)

↑ Increase / Stimulate
Increase water / secretion
→ Result / leads to
ENS: Enteric Nervous System

Drugs Affecting GI Motility

Laxative Agents.

Nonpharmacologic Remedies

- High fiber diet.
- Adequate fluid intake.
- Regular exercise.
- Responding to nature's call.

Bulk-Forming Laxatives

- Are indigestible, hydrophilic colloids that absorb water, forming a bulky, emollient gel that distends the colon and promotes peristalsis.
- Can cause **bloating** and **flatus**.

Natural Plant Products
- Psyllium
- Sterculia "Normacol"
- Methylcellulose

Synthetic Fibers
- Polycarbophil

Stool Surfactant Agents(Softeners)

- They permit water and lipids to penetrate.
- Given orally or rectally.
- Docusate
- Glycerin suppository
- Mineral oil
  - Aspiration can cause lipoid pneumonia.
  - Can impair absorption of fat-soluble vitamins

Osmotic Laxatives (Purgatives)

- Soluble nonabsorbable compounds that result in increased stool liquidity due to an obligate increase in fecal fluid

- Magnesium oxide (Milk of Magnesia)
  - Can cause **hypermagnesemia**.
  - Large doses of magnesium citrate and sodium phosphate can cause Purgation: rapid bowel evacuation within1-3 hours. This might cause **volume depletion**.
- Sorbitol
- Lactulose
  - Sugars metabolized by bacteria producing severe flatus and cramps
- Balanced Polyethylene Glycol
  - Safe solution: no intrvascular fluid or electrolyte shifts. Does not cause cramps or flatus.
  - Used for complete colonic cleansing before endoscopy.
  - PEG is an inert, nonabsorbable, osmotically active sugar.

For colonic cleansing, it should be ingested rapidly(4 L over 2-4hs).
For chronic constipation, PEG powder is mixed with water or juice.

Stimulant Laxatives (Cathartics)

- Direct stimulation of the enteric system.
- Colonic electrolyte and fluid secretion.

Adverse effects:- Can lead to dependence and destruction of the myenteric plexus resulting in colonic atony and dilation.

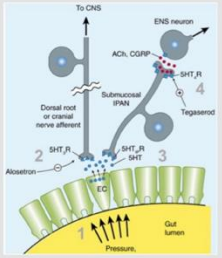
- May be needed in neurologically impaired patients and in bed-bound patients in long term care facilities.

بنعطيها للناس اللي عندهم مشاكل في الأعصاب (يعني أمعاؤهم ما بتتحرك منيح).
كمان بنعطيها للناس اللي نايمين بالفراش لفترة طويلة (مثل المرضى في دور الرعاية).
لأنهم ما بيتحركوا كتير، فأمعاؤهم بتكسل، فبنحتاج شي "ينبّهها" تتحرك وتشتغل.

- Anthraquinone Derivatives
  - Poorly absorbed .
  - After hydrolysis, produce bowel movement in (6-12) hours.
  - Cause brown pigmentation of the colon" Melanosis Coli".
  - Not carcinogenic
  - Aloe
  - Senna
  - Cascara
- Castor oil
  - Hydrolyzed in upper intestine into ricinoleic acid which is a local irritant.
  - Was used as purgative to clean the colon before procedures

Antidiarrheal Agents

Tegaseroid



مشان نعرف الـ MOA اله ، لازم نعرف الحالة الطبيعية بالبداية <=
1 أول شي:
لما الأمعاء تنتفخ (تمتلي بالأكل أو الغازات)،
خلايا خاصة فيها اسمها EC cells بتفرز مادة اسمها
(سيروتونين) 5-HT
2 بعدين:
5-HT
بيروح يحفّز نوعين من الأعصاب
✅ النوع الأول:
5-HT3 receptors
موجودين على أعصاب بتوصّل للدماغ، لما يتنشّطوا ممكن يصير:
وجع بطن / غثيان / استفراغ
✅ النوع الثاني:
5-HT1P receptors
موجودين داخل الأمعاء، على أعصاب اسمها IPANs، هاي الأعصاب بتنشّط (enteric neurons)
إلّي بيؤدي إلى :
حركات الأمعاء (peristalsis) / إفرازات الهضم
3 وأخيرًا:
5-HT4 receptors
كمان موجودين على الأعصاب داخل الأمعاء، لما يتنشّطوا، بيساعدوا الأعصاب تفرز مواد: ACh && CGRP
وهاي المواد بتقوّي حركة الأمعاء أكتر وأكتر.
النتيجة: الأمعاء تتحرك بشكل طبيعي، تدفع الأكل، وتهضم، وتخلّص الفضلات.

Tegaserod:
- Is a serotonin 5-HT4 partial agonist, which are presynaptic receptors of the submucosal intrinsic primary afferent nerves which enhance the release of their neurotransmitters.
- These neurones stimulate proximal bowel contraction(via ACh and substance P) and distal relaxation(via nitric oxide and VIP).
- The drug promotes gastric emptying and small and large bowel transit but has no effect on esophageal motility.
- Also stimulates cAMP-dependent chloride secretion leading to increased stool liquidity.

Clinical Uses
- Chronic constipation
- Nonulcer dyspepsia.عسر الهضم بدون قرحة
- Gastroparesis تأخر إفراغ المعدة
- Irritable bowel syndrome.

Adverse Effects
Diarrhea occurs in 9% of patients within days.

Extremely safe drug.
Expensive

This mind map done by
Toleen Mawazrah (Doctor 023)

Antidiarrheal Agents

Antidiarrheal Agents

- Unlike laxatives, antidiarrheal drugs are **used to reduce or stop diarrhea.**
- **Can be used in mild to moderate acute diarrhea.**
- **Should not be used in the presence of infective diarrhea ,** because diarrhea serves as a **protective mechanism** that helps the body to eliminate pathogens such as bacteria and viruses; Suppressing diarrhea in these cases may prolong the infection and **worsen its effects on the body.**
- **Can be used to control chronic diarrhea** associated with certain syndromes & pathological conditions **, like in irritable bowel syndrome or inflammatory bowel disease** , where patients may experience recurrent episodes of diarrhea alternating with constipation ; therefore, anti- diarrheal drugs may be used occasionally when needed.

Antidiarrheal Agents

Opioid Agonists: (Their use is limited because of the risk of dependence)

Have significant constipating effects:

- **Inhibit presynaptic cholinergic nerves, leading to increased colonic transit time** (The contents remain in the colon for a longer period of time) **and increased fecal water absorption.**
- **Decrease mass colonic movements and** thus they reduce the **gastrocolic reflex.**
- **Can have CNS effects and addiction potential.**(That's why their use is limited)
- **Usually combined with atropine to reduce dependence** , as one of the methods used **to reduce the addiction it may cause.**

Antidiarrheal Agents

Opioid Agonists:

Loperamide:

- **Does not cross BBB.**
- **No analgesic or addiction potential** , so it is preferred as opioid agonists over diphenoxylate.

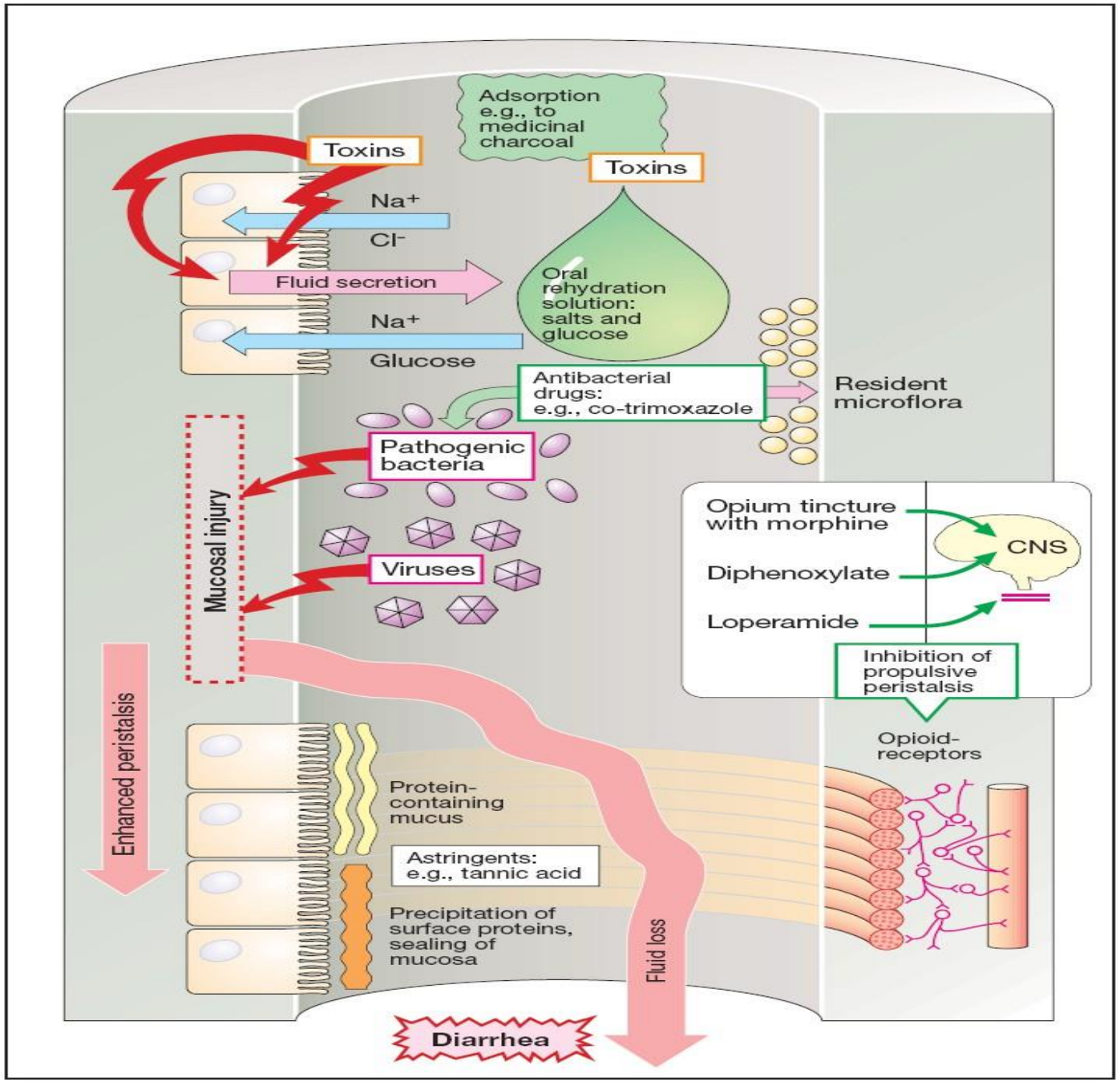
Diphenoxylate:

- Like a classical opioid agonist so it **Can have CNS effects and dependence.**
- combined with atropine to reduce dependence .

This diagram provides a general overview of antidiarrheal agents. As we continue, we will notice that many of these drugs have already been discussed in details.

As a general idea:

- Some agents, such as charcoal, work by adsorbing toxins present in the bowel that may trigger diarrhea.
- Other agents, such as the antibacterial drug co-trimoxazole help reduce bacterial infections responsible for inducing diarrhea.



A. Antidiarrheals and their sites of action

Antidiarrheal Agents

Kaolin and Pectin:

- **Kaolin is a naturally occurring hydrated magnesium silicate.**
- **Pectin is an indigestible carbohydrate derived from apples** peel**.**
- **Both act to absorb bacteria, toxins and fluid** , so that helps reduce toxin absorption in toxin associated diarrhea.
- **Usually combined, e.g. Kaopectate.** (Most often , they are used together in a formulation known as **kaopectate**)
- This combination helps in toxin associated diarrhea by absorbing the toxins in the gut rather than directly stopping diarrhea.
- **Taken far from other medications.**

Antidiarrheal Agents

Note: treatment of diarrhea depends on understanding its underlying causes .

Malabsorption of bile salts (e. g .after surgical resection), can cause diarrhea.

Bile salt-binding resins:

Cholestyramine

Colistipol.

- **The drugs can bind bile salts** and this helps stop diarrhea caused by bile salts malabsorption.

Drugs side effects:

- **Can cause bloating, flatulence, constipation and fecal impaction.**
- **Also, drug and fat malabsorption.** (There is a note in the next slide)

- **drug and fat malabsorption.**

Note on the lecture clarifications:

It was mentioned in the lecture that bile salt binding resins may also bind to fat; however, **this is not entirely accurate**.In reality, drugs such as Bile salts binding resins **bind only to bile salts** in the intestine and prevent their reabsorption. They do not directly bind to dietary fat. By reducing available bile salts, **fat digestion is impaired**, which indirectly leads to fat malabsorption.

Recall :Bile salts emulsify fats and help form micelles for absorption. Without them, fat digestion and absorption are impaired

Antidiarrheal Agents

Octreotide:

Is a synthetic octapeptide with actions similar to somatostatin.

Somatostatin is a 14 amino acid peptide released in the GIT and pancreas as well as from the hypothalamus:

1. **Inhibits release of many hormones.**
2. **Reduces intestinal fluid and pancreatic secretions.**
3. **Slows GIT motility and gallbladder contraction.**
4. **Contracts blood vessels.**
5. **Inhibits secretion of some anterior pituitary hormones.**

Helpful notes for understanding

Main idea:
It acts like a **"brake"** for the body → slows everything down.

Meaning:
Secretions decrease ↓
Intestinal movement slows down ↓
Hormone release decreases ↓

This is useful in diarrhea because diarrhea usually involves:

- rapid intestinal movement
- excessive fluid secretion

So the drug reduces both.

Antidiarrheal Agents

Octreotide:

Clinical Uses:

1. **Inhibition of endocrine tumor effects:**
   Carcinoid can cause secretory diarrhea and systemic symptoms like flushing and wheezing.
2. **Diarrhea due to *vagotomy or *dumping syndrome or and AIDS.**
3. **In small doses can stimulate motility in small bowel bacterial overgrowth or intestinal pseudo-obstruction secondary to *scleroderma.**
4. **pituitary tumors and GI bleeding.**

***vagotomy** usually means cutting the branch of the vagus nerve that tells your stomach to secrete gastric acid

***Dumping syndrome** is a condition in which food, especially food high in sugar, moves from your stomach into your small bowel too quickly after you eat

***Scleroderma** is an uncommon condition that results in hard, thickened areas of skin

Key summary for quick revision ;)

ANTI-DIARRHEAL DRUGS

GOAL: Reduce stool frequency and improve consistency

1 OPIOID AGONISTS

Examples

- Loperamide
- Diphenoxylate (+ Atropine)

MOA

- Act on μ-opioid receptors in the gut
- ↓ GIT motility
  - → ↑ transit time
  - → ↑ water absorption

Key points

- Loperamide does not cross BBB → No CNS effects, No addiction (preferred)
- Diphenoxylate may cross BBB → CNS effects & dependence
- Often combined with atropine to reduce abuse

2 ADSORBENTS

Examples

- Kaolin
- Pectin

MOA

Absorb:

- toxins
- bacteria
- fluid

} Form a protective coating

Use

Toxin-associated diarrhea

Key points

- Do not stop motility
- Take at different time from other medications

3 BILE SALT–BINDING RESINS

Examples

- Cholestyramine
- Colestipol

MOA

Bind bile salts in the intestine

→ Prevent irritation of colon

→ Reduce diarrhea

Use

Diarrhea due to bile salt malabsorption (e.g. after ileal resection, cholecystectomy)

Side effects

- Bloating, flatulence
- Constipation, fecal impaction
- Fat & drug malabsorption

4 SOMATOSTATIN ANALOG

Example

- Octreotide

Main idea

"GI brake" → slows everything down

Effects

- ↓ Hormone release
- ↓ Intestinal & pancreatic secretions
- ↓ GIT motility & gallbladder contraction
- ↓ Blood flow (vasoconstriction)

Uses

- Secretory diarrhea (e.g. carcinoid syndrome)
- Vagotomy or dumping syndrome
- AIDS-related diarrhea
- GI bleeding
- Pituitary tumors (↓ GH)

WHY DIARRHEA HAPPENS?

- ↑ Motility
- ↑ Secretion
- Toxins / Infection
- Bile salt irritation

HOW DRUGS HELP?

Slow movement + Reduce secretion + Absorb toxins + Bind bile salts = Less diarrhea

GENERAL NOTES

- Do not use in infective diarrhea (it is a protective mechanism).
- Use with caution in chronic diarrhea due to IBS or IBD.

Always treat the cause when possible & maintain hydration!

Drugs Used in the Treatment of Irritable Bowel Syndrome(IBS)

IBS is an idiopathic chronic, relapsing disorder characterized by: Abdominal discomfort (irritable conditions)

pain, bloating, distention, or cramps with alterations in bowel habits

diarrhea, constipation, or both

Pharmacologic therapies for **IBS** are directed at relieving abdominal pain and discomfort and improving bowel function.

Drugs used in Irritable Bowel Syndrome

- **Antispasmodic or Anticholinergic Agents:**(first line of treatment)
  - **Dicyclomine**
  - **Hyoscyamine.**
    - **Spasm is not an important symptom in IBS.**
    - **They inhibit muscarinic cholinergic receptors in the enteric plexus and on smooth muscle** of the intestine**.**
    - **At usual low doses**(recommended doses)**, have minimal side effects.**

Side effects will be directed to over anticholinergic effects (in high doses)

Drugs used in Irritable Bowel Syndrome

- **Serotonin 5-HT_3- Receptor Antagonists:**
  - **Alosterone:**
    - **5-HT_3 receptors are present in the afferent pain fibers in the extrinsic sensory neurons. Also present on the terminals of the enteric cholinergic neurons. Centrally, 5-HT_3 is involved in the central response to visceral afferent stimulation.**

Helpful notes for understanding

- **Serotonin 5-HT_3- Receptor , Where are they located?**

1)Afferent sensory nerves (gut → brain)
Found on extrinsic visceral afferent neurons .These nerves carry pain and distension signals from the gut to the CNS
Function: transmit abdominal pain and discomfort
2)Enteric nervous system
Located on cholinergic neurons in the gut wall .Regulate intestinal motility & secretion
Function: control gut movement and fluid secretion
3)Central nervous system (brainstem)
Involved in the vomiting center and visceral sensory processing
Function: mediates nausea and vomiting response

- **What do 5-HT3 receptor antagonists do?**

They **block serotonin action at 5-HT3 receptors** in all these locations.

- **By blocking these receptors, they:**

↓ transmission of visceral pain signals
↓ gastrointestinal secretion and abnormal motility
↓ nausea and vomiting

Lec 3

Drugs Affecting GI Motility

Laxative Agents.

Antidiarrheal Agents

~ Can be used in mild to moderate acute diarrhea.
~ Should not be used in the presence of infective diarrhea.
~ Can be used to control chronic diarrhea, like in irritable bowel syndrome or inflammatory bowel

Opioid Agonists

MOA

Inhibit presynaptic cholinergic nerves
→ ↓ peristalsis
→ ↓ mass colonic movements and gastrocolic reflex.
→ ↑ colonic transit time
حتى يُمتص سوائل قدر المستطاع في وقت اكثر
→ ↑ fecal water absorption
– – – – – – – – – – – – – –
Can have CNS effects and addiction potential.
Usually combined with atropine to reduce dependence

Examples
- Loperamide
  - Does not cross BBB.
  - No analgesic or addiction potential.
- Diphenoxylate
  Can have CNS effects and dependence.

Adsorbents

~ act to absorb bacteria, toxins and fluid.
~ Usually combined, e.g. Kaopectate.
~ Taken far from other medications.
(to avoid absorption of other drugs)

Examples
- Kaolin
  a naturally occurring hydrated magnesium silicate.
- Pectin
  indigestible carbohydrate derived from apples

Bile salt-binding resins

Theses drugs can bind bile salts in cases of Malabsorption of bile salts (e. g .after surgical resection), which can cause diarrhea.
Adverse effects:- bloating, flatulence, constipation and fecal impaction. Also, drug and fat malabsorption.

Examples
- Cholestyramine
- Colistipol

vagotomy usually means cutting the branch of the vagus nerve that tells your stomach to secrete gastric acid.
Dumping syndrome is a condition in which food, especially food high in sugar, moves from your stomach into your small bowel too quickly after you eat.
Scleroderma is an uncommon condition that results in hard, thickened areas of skin

Octreotide

Is a synthetic octapeptide “8” with actions similar to somatostatin.
Somatostatin is a 14 amino acid peptide released in the GIT and pancreas as well as from the hypothalamus:
1. Inhibits release of many hormones.
2. Reduces intestinal fluid and pancreatic secretions.
3. Slows GIT motility and gallbladder contraction.
4. Contracts blood vessels.
5. Inhibits secretion of some anterior pituitary hormones.

Clinical uses
- Inhibition of endocrine tumor effects: Carcinoid can cause secretory diarrhea and systemic symptoms like flushing and wheezing.
- Diarrhea due to vagotomy or dumping syndrome or and AIDS.
- In small doses can stimulate motility in small bowel bacterial overgrowth or intestinal pseudo-obstruction secondary to scleroderma.
- pituitary tumors and GI bleeding.

IBS is an idiopathic **chronic, relapsing** disorder characterized by: Abdominal discomfort pain, bloating, distention, or cramps with alterations bowel habits diarrhea, constipation, or both. therapies for IBS are directed at relieving abdominal pain and discomfort and improving bowel function. ما بتعالج المرض، بتخفف الأعراض فقط

Drugs Used in the Treatment of Irritable Bowel Syndrome

Antispasmodic or Anticholinergic Agents.

- Spasm is not an important symptom in IBS.
- They inhibit muscarinic cholinergic receptors in the enteric plexus and on smooth muscle.
- At usual low doses, have minimal side effects.

Examples:
- Dicyclomine
- Hyoscyamine

Serotonin 5-HT3-Receptor **Antagonists**

Alosterone

5-HT3 receptors are present in the afferent pain fibers in the extrinsic sensory neurons.
Also present on the terminals of the enteric cholinergic neurons. Centrally, 5-HT3 is involved in the central response to visceral afferent stimulation.

- Selective antagonist of 5-HT3 receptors.
- Has long duration of action.
- Approved for women with severe IBS in whom diarrhea is the prominent symptom.
- Efficacy in men is not established.
- Can cause ischemic colitis, severe constipation requiring hospitalization and surgery(occurs when blood flow to part of the large intestine is temporarily reduced)

Serotonin 5-HT3-Receptor **Agonists**

Tegaserod

- Approved for short term treatment of women with IBS who predominantly have constipation.
- Reduces pain, bloating and hardness of stool.
- Expensive.

رسالة من الفريق العلمي:

(قَالَ أَخَرَقْتَهَا لِتُغْرِقَ أَهْلَهَا)

يحمِيكَ اللهُ بطُرُقٍ لا تَفهَمُها
ستُخرَقُ لكَ سُفُن،
لأنّ الله يريدُ أنْ يحمِيكَ من إبحارٍ خاطئٍ
ستتعثَّرُ لك خطىً،
لأنّ الله يريدك ألّا تبلغَ وُجْهةً مُؤذيةً
وستفُوتُ عليكَ فُرَصٌ،
لأنّ الله يُعطيك ما تحتاجُه لا ما تُريده
وستُصْفَعُ على وجهِكَ،
لأنّها الطَّريقةُ الوحيدةُ كي تستفيقَ من غفلتِكَ
وسيُكسَرُ قلبُكَ،
لأنَّ كسّرَ القلبِ أوّل خطواتِ الأَنسِ باللهِ،
الكثيرُ من الحِماية يأتي مقرُوناً بالوجع!

من كتاب و بالحقّ أنزلناه - أدهم شرقاوي

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 7	One information has been added	PEG + added electrolytes =**Balanced GEG** which is very safe solution without intravascular fluid or electrolytes shift
V1 → V2			