Anti-diarrheal agents

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Common Causes of Sudden or Chronic Diarrhea

Sudden Diarrhea

Food poisoning

Traveler's diarrhea

Stomach flu

Chronic Diarrhea

Celiac disease

Food intolerance/ allergy

Milk/soy protein intolerance

IBS

Medication

verywell

Pathophysiology of diarrhea

- Increase the GIT motility
- Increase the secretions and decrease the absorption of fluids and electrolytes ----------which lead to Na , water and electrolyte disturbance
- Infection

Treatment of diarrhea

A- Rehydration (oral or I.V fluids)

B- Anti-infective agents (according to infective organism)

C- Non-antimicrobial antidiarrheal agents

D-Treatment of inflammatory bowel diseases

C- Non-antimicrobial antidiarrheal agents:

should not be used in patients with

1-bloody diarrhea

2-high fever

3- systemic toxicity

because of the risk of worsening underlying condition.

N.B: you should stop if worsen despite therapy

They are classified as follow:

1-Anti-motility agents

2-GIT protective & adsorbents agents

3-Agents which modify fluid and electrolyte transport

4-Others

-Bile salts binding resins (cholestyramine)

1- Antimotility agents

A-Anticholinergic (they reduce the motility and secretions of the GIT as atropine and propantheline)

B-Opioid agonists (they activate μ receptors on enteric neurons → ↑ K^+ efflux → hyper polarization → inhibit Ach release →↓motility →↑ transit time → ↑absorption of fluid & electrolyte.

Diphenoxylate:

- Readily absorbed → systemic effects (sedation & addiction).
- **Lomotil:** Diphenoxylate + atropine .

Loperamide (Imodium):

- Slow & incomplete absorption.
- Not crossing B.B.B.
- Relatively selective action on G.I.T.

- **Side effects:**

➢Dry mouth, dizziness, headache, abdominal cramps, nausea and vomiting.

➢Paralytic ileus.

- **Contraindications:**

➢Chronic ulcerative colitis.

➢Young children.

➢Acute bacillary & amoebic dysentery.

2-GIT protective & adsorbents agents:

- Kaolin.
- Pectin.
- Chalk.
- Methylcellulose.
- Charcoal.

Kaopectate (kaolin & pectin):

- 1.2-1.5 g after each loose bowel movement (maximum: 9g /d).
- Not absorbed **(no adverse effects).**
- Should not be taken within **2 hours** of other medication.

3-Agents which modify fluid and electrolyte transport:

Reduce secretion & or stimulate absorption of fluids

Bismuth subsalicylate

[Bi^{3} (antibacterial) + salicylate (inhibit PG)]:

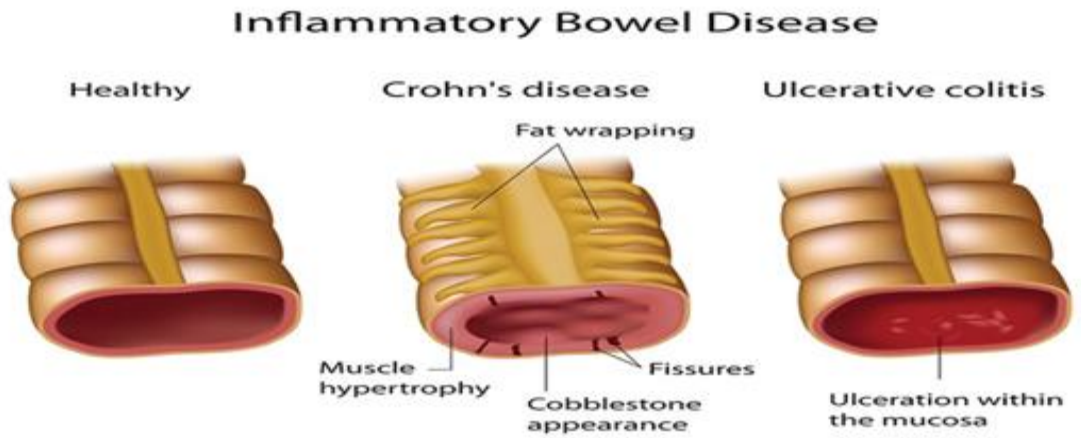
- Coat ulcer.
- ↓ Stool frequency & liquidity in acute infectious diarrhea, due to salicylate inhibition of intestinal PG & chloride secretion.

- ✓ Bismuth has direct antimicrobial effects & binds enterotoxins.
- ✓ Prevent & treat **traveler's diarrhea**
- ✓ Bismuth compound have direct antimicrobial activity **against H pylori.**
- ✓ **Dose:** Pepto-Bismol; 2 tablets (520mg) every 30 min.

Chronic inflammatory bowel disease (IBD) includes:
(ulcerative colitis & Crohn's disease).

Drugs used in treatment of IBD include:

- **Corticosteroids:** prednisolone.
- **Immunosuppressive agents:** azathioprine , 6mercaptopurine.
- **Aminosalicylates.**



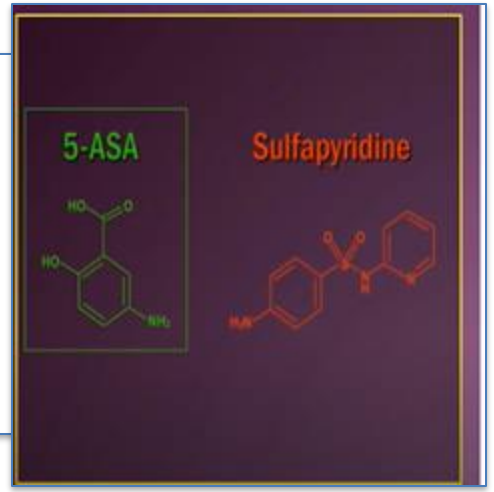
Aminosalicylates

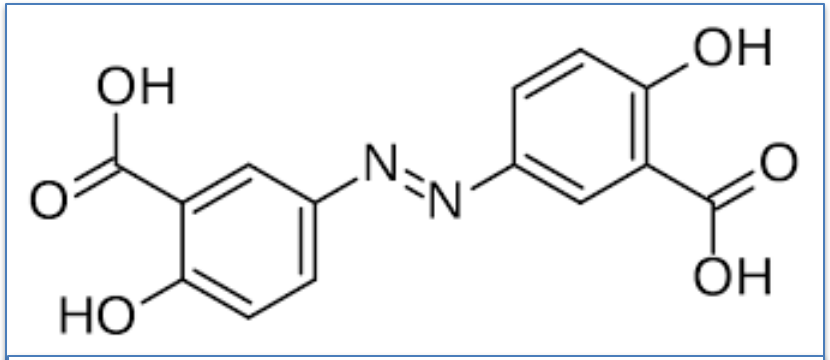
Up to 80% of unformulated, aqueous 5-ASA is absorbed from the small intestine & does not reach the distal small bowel or colon in appreciable quantities.

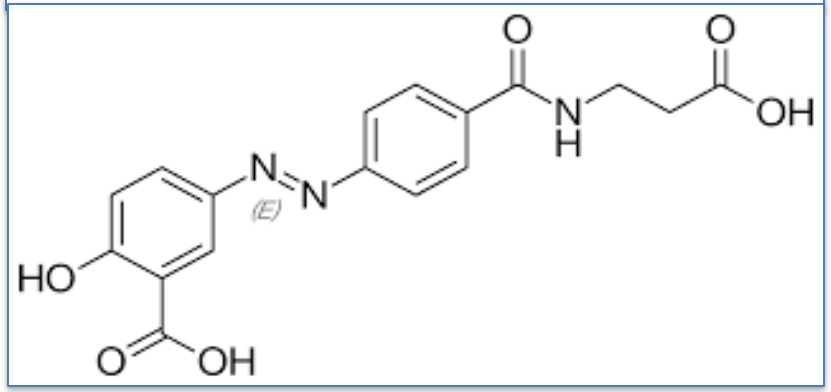
❑ Azo compounds:

- 5-ASA bound by an azo (N=N) bond to an inert compound or to another 5- ASA molecule.
- Azo markedly reduces absorption of the parent drug f rom the small intestine.
- In terminal ileum & colon, bacteria cleave the azo bond by azo reductase, releasing the active 5-ASA.

- **Sulfasalazine:** (5-ASA "Active moiety" +Sulfapyridine "side effects").
- **Olsalazine:** (two molecules of 5-ASA).
- **Balsalazide:** (5-ASA + 4-aminobenzol-β- alanine).







Mesalamine compounds

Package of 5-ASA itself in various ways to deliver it to different segments of the small or large bowel.

Pentasa: contains timed-release microgranules that release 5- ASA throughout the small intestine.

Asacol: has 5-ASA coated in pH-sensitive resin that dissolves at pH 7 (the pH of the distal ileum & proximal colon).

Rowasa (enema formulations) &

Canasa (suppositories): To deliver high concentration of 5-ASA to the rectum & sigmoid colon.

Mechanism of action:

- ✓ 5-ASA inhibits inflammatory mediators derived from both the cyclooxygenase &lipooxygenase pathways.
- ✓ Interferes with the production of inflammatory cytokines.
- ✓ Inhibits the activity of nuclear factor-k_B (NF-k_B), an important transcription factor for pro-inflammatory cytokines.
- ✓ Inhibits cellular functions of natural killer cells, mucosal lymphocytes, and macrophages.
- ✓ It may scavenger reactive oxygen metabolites.

Pharmacokinetics:

Mesalamine:

- 20-30% of 5-ASA is absorbed.
- 5-ASA undergoes N-acetylation in the liver and gut epithelium.
- Metabolite is excreted by the kidneys.

Sulfasalazine

- 10% is absorbed.
- After azoreductase, >85% of sulfapyridine is absorbed.
- Sulfapyridine undergoes hepatic metabolism.
- Metabolite is excreted by the kidney.

Balsalazide:

- <1% is absorbed.
- After azoreductase, small amount of systemic absorption occurs.

Therapeutic uses:

1. First-line agents for treatment of mild to moderate active ulcerative colitis
2. Crohn's disease involving the small bowel ***mesalamine*** compounds, which release 5-ASA in the small intestine, have advantage over azo compounds

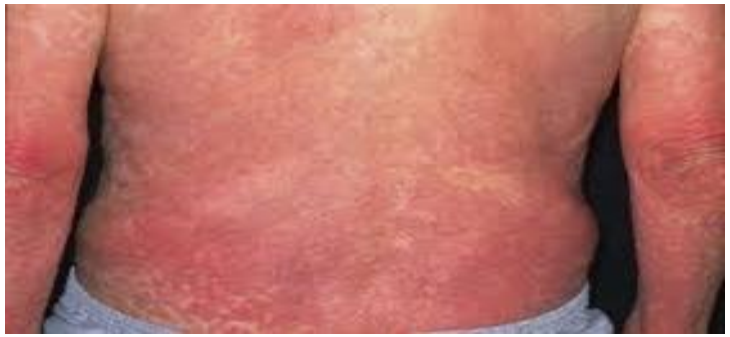
3. Ulcerative colitis or Crohn’s colitis that extends to the proximal colon, both azo & mesalamine compounds are useful.

3. Ulcerative colitis or Crohn’s disease confined to the rectum or distal colon, suppositories or enema are useful.

Adverse effects:

Sulfasalazine (→ sulfapyridine) has high incidence of side effects , >40% cannot tolerate therapeutic doses:

1. GIT upset, headache, arthralgia, bone marrow suppression & malaise
2. Hypersensitivity (fever, exfoliative dermatitis, pancreatitis, pneumonitis, hemolytic anemia, pericarditis, or hepatitis).
3. Reversible oligospermia
4. Impairs folate absorption



Other aminosalicylate formulations

Are well tolerated:

Olsalazine may cause secretory diarrhea (10%).

Hypersensitivity (rare).

Interstitial nephritis (rare, high doses of ***mesalamine***).


THANK YOU