

1. GI Pharmacology: Drugs for Constipation & Diarrhea

# GI Pharmacology: Drugs for Constipation & Diarrhea

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2. Objectives

## Objectives

- Illustrate drug mechanisms of action
- Identify most common drug side effects
- Provide examples of each drug type

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### Drugs for Constipation

## Drugs for Constipation

- **Bulk forming agents**
  - Psyllium, Methylcellulose, Polycarbophil
- **Softeners/surfactants**
  - Docusate, Mineral oil
- **Osmotic agents**
  - Saline-based
  - Sugar/alcohol-based
  - Other (PEG solutions)
- **Stimulants**
  - Bisacodyl, Senna, Cascara
- **Miscellaneous**
  - Lubiprostone; Tegaserod

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### Bulk-forming Agents

## Bulk-forming Agents

- **Mechanisms:**
  - Source of fiber
    - Enhances stool mass
- **Main concerns/toxicities:**
  - Bloating & abdominal pain
    - Avoid if suspect obstruction
  - Drug interactions of absorption

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## Bulk-forming Agents

### Bulk-forming Agents

- **Examples:**
  - Natural
    - Psyllium
  - Semi-synthetic
    - Methylcellulose
    - Polycarbophil

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## Softeners/Surfactants

### Softeners/Surfactants

- **Mechanisms:**
  - Lowers surface tension of stool
- **Main concerns/toxicities:**
  - Specific to mineral oil
- **Examples:**
  - Docusate
  - Mineral oil

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## Osmotic Agents

### Osmotic Agents

- Mechanisms:
  - Osmotically-mediated water retention stimulates peristalsis
- Main concerns/toxicities:
  - Abdominal distension, flatulence
  - For saline-based caution if:
    - Renal or cardiovascular disease
    - Underlying electrolyte disorders or on diuretics
    - Monitor Mg, Phos, K, Na, Ca

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## Osmotic Agents

### Osmotic Agents

- Examples:
  - Saline-based:
    - Magnesium citrate
    - Phosphate salts
  - Sugar/alcohol-based:
    - Lactulose, Sorbitol, Mannitol
    - Glycerin (suppositories/enemas)
  - Other:
    - Polyethylene glycol (PEG) solutions

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## Stimulant Laxatives

### Stimulant Laxatives

- Mechanisms:
  - Produce migrating colonic contractions
- Concerns/toxicities:
  - Avoid overuse
  - Phenolphthalein and Danthron-containing products banned by FDA in 1999

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## Stimulant Laxatives

### Stimulant Laxatives

- Examples:
  - Diphenylmethanes
    - Bisacodyl
      - Onset of action oral vs rectal
  - Anthraquinones
    - Aloe
    - Cascara
    - Senna
  - Castor oil

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## Miscellaneous Agents

### Miscellaneous Agents

- **Lubiprostone**
  - **Mechanism:**
    - Activates chloride channels within GI tract
      - Increasing intestinal fluid secretion
  - **Concerns/toxicities:**
    - Nausea
    - Abdominal distension & pain
    - Diarrhea & flatulence
    - Headache
    - Avoid in pregnancy

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13. Anti-diarrheals

## Anti-diarrheals

- **Bulk forming & binding agents**
  - Psyllium, Methylcellulose, Polycarbophil
  - Cholestyramine
  - Bismuth
- **Antimotility agents**
  - Opioids & derivatives
- **Antisecretory agents**
  - Octreotide
- **Miscellaneous**
  - Clonidine; Alosetron

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14. Bulk-forming & binding agents

## Bulk-forming & binding agents

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15. Bulk-forming & binding agents

## Bulk-forming & binding agents

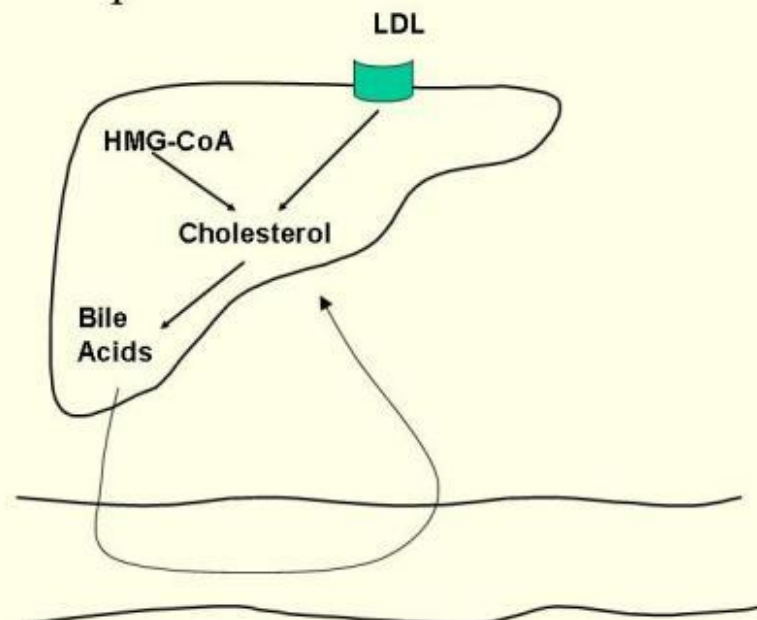
- Examples:
  - Natural
    - Psyllium
  - Semi-synthetic
    - Methylcellulose
    - Polycarbophil
  - Other agents:
    - Cholestyramine
    - Bismuth subsalicylate

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16. Enterohepatic Recirculation of Bile Acids

## Enterohepatic Recirculation of Bile Acids



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Adapted from: Hardman JG, Limbird LE, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York: McGraw-Hill, 2001.

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## Bile Acid Sequestrants

### Bile Acid Sequestrants

- Adverse effects:
  - Few systemic
  - Primarily GI-related
    - Abdominal pain, bloating, constipation
  - Tooth discoloration
    - Liquids
  - Reduced absorption of fat soluble vitamins

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## Antimotility Agents

### Antimotility Agents

- Opioid derivatives:
  - Diphenoxylate + Atropine
    - High doses (40-60 mg) required to produce analgesia
  - Loperamide
    - Little/no penetration into CNS

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## Other Opioid Derivatives

### Other Opioid Derivatives

- Camphorated tincture of opium  
Morphine 0.4 mg/mL
- Deodorized tincture of opium  
Morphine 10 mg/mL

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## Miscellaneous Agents

### Miscellaneous Agents

- Clonidine
  - Centrally acting alpha-2 receptor agonist
- Alosetron
  - 5HT<sub>3</sub> receptor antagonist
    - For women
    - When primary symptom is diarrhea
    - Use restricted due to side effect concerns (ischemic colitis)

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