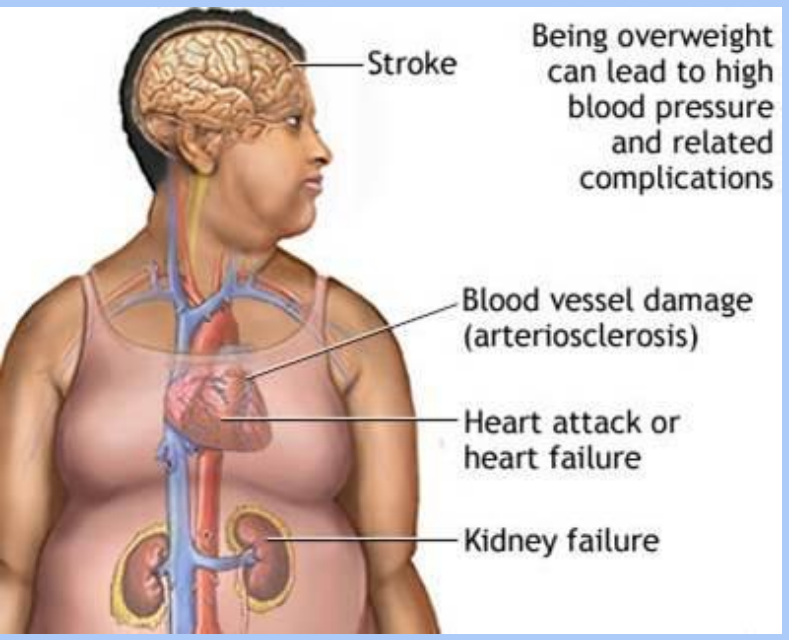
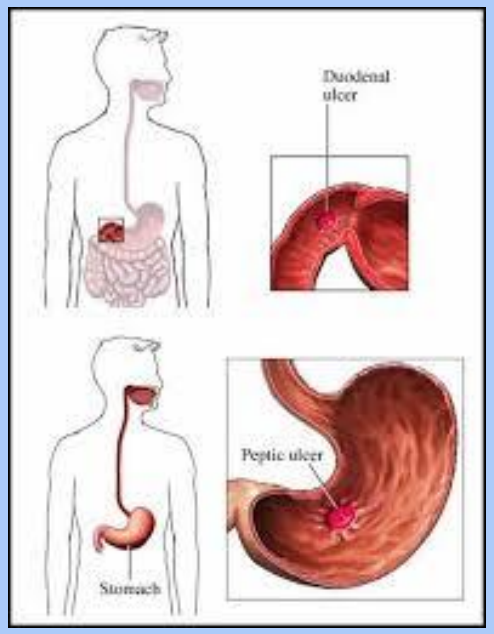
Zaporozhye State Medical University
Pharmacology and Medical Formulation Department

Lecture № 10

Drugs Used to treat Gastrointestinal Diseases





Agents Stimulating the Appetite:

1. Bitters: Wormwood tincture –

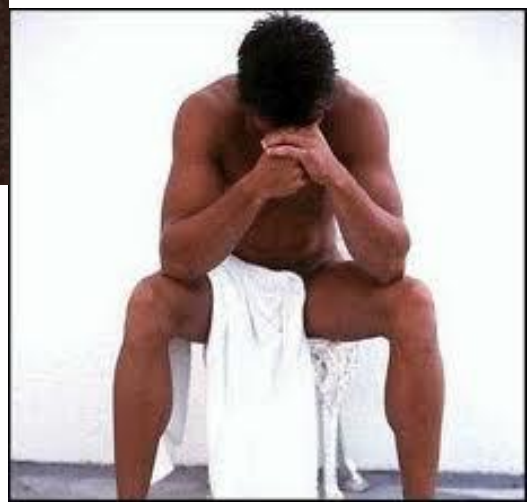
Tinctura Absinthii - *vial 25 ml:*

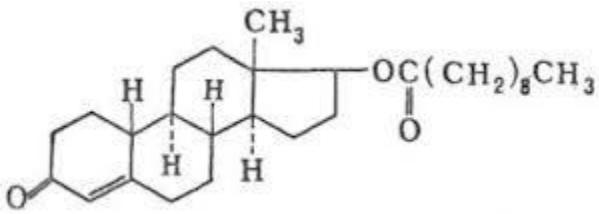
PO 15-20 drops 15-20 min before meals tid

2. Others: Insulin, Vitamins,

Anabolic Steroids: Retabolil

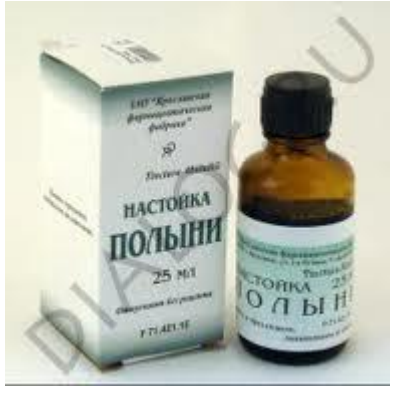
Phenoboline





Wormwood tincture contains glycoside *Absinthian* and *Ethereal Oil* composed of *Terpenes* and a camphor isomer *Absenthol*.

Bitters stimulate receptors of oral cavity mucous and increase the excitability of **Starvation's Center** located at **Lateral Nucleus of Hypothalamus**.



Agents Inhibiting Appetite

Appetite Suppressants – **Anorexigenic agents**:

1. **Centrally acting adrenergic agents** – stimulating the CNS:

   Phenamine (***Amphetamine***)

   Phepranone (dr. 0.025 g)

2. **Centrally acting serotoninergic agonist**:

   Fluoxetine (*Prozac* – tab. 0.02 g)

3. **Centrally acting agents** on **both adrenergic** and **serotoninergic** systems – **depressing** the CNS:

   Sibutramine (caps. 5 and 10 mg)

Drugs Used to Treat Peptic Ulcer Disease

I. Inhibitors of Gastric Acid Secretion:

1. Proton Pump Inhibitors:

Omeprazole (caps. 0.02 g)
Lansoprazole (caps. 0.03 g)
Pantoprazole (tab. 0.04 g)
Rabeprazole (tab. 0.01 and 0.02 g)

2. H_2-Histamine Receptor Blockers:

Cimetidine (amp. 10%-2 ml, tab. 0.2 g)
Famotidine (tab. 0.02 and 0.04 g)
Ranitidine (tab. 0.15 g)

3. M-Cholinoblockers:

Atropine sulfate (amp. 0.1%-1 ml, tab 0.5 mg)
Platyphyllin hydrotartrate (amp. 0.2%-1 ml, tab. 0.005 g)
Pirenzepine (*Gastrozepin* – tab. 0.025 and 0.05 g)

II. Gastroprotectors:

1. Producing Mechanical Defense of Mucous Coat:

Sucralfate (***Venter*** – tab. 0.5 g)

Bismuth tripotassium dicitrate (***De-nol*** - tab. 0.12 g)

2. Increasing Protective Function of the Mucus Barrier :

- PG analogues:

Misoprostol (***PG E_1*** – tab. 0.2 mg)

Enprostil (***PG E_2*** – caps. 35 mg)

Arbaprostil, Rioprostil

- Others: **Carbenoxolone** (***Biogastrone*** – tab. 150 mg)

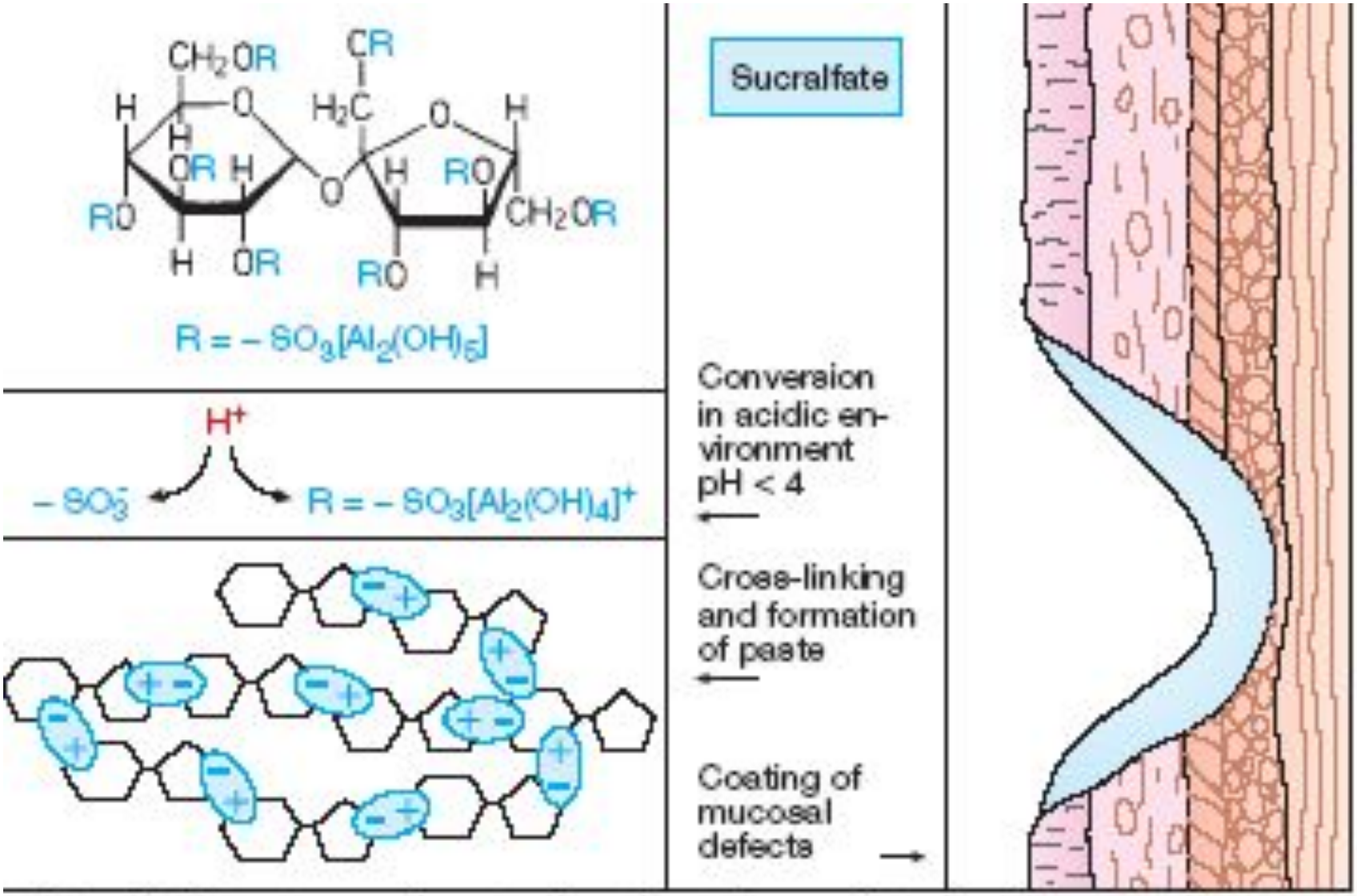
Dalargin (amp. 0.001 g)

III. Antimicrobial Agents – Suppressing *Helicobacter pylori* - infection:

Amoxicilline (tab. 0.25 and 0.5 g)

Clarithromycin (tab. 0.5 g)

Metronidazole , Tetracycline



. Chemical structure and protective effect of sucralfate

IV. ANTACIDS:

Aluminium hydroxide (pulv. 0.25-1.0 g)

Almagel (vial 170 ml)

Maalox

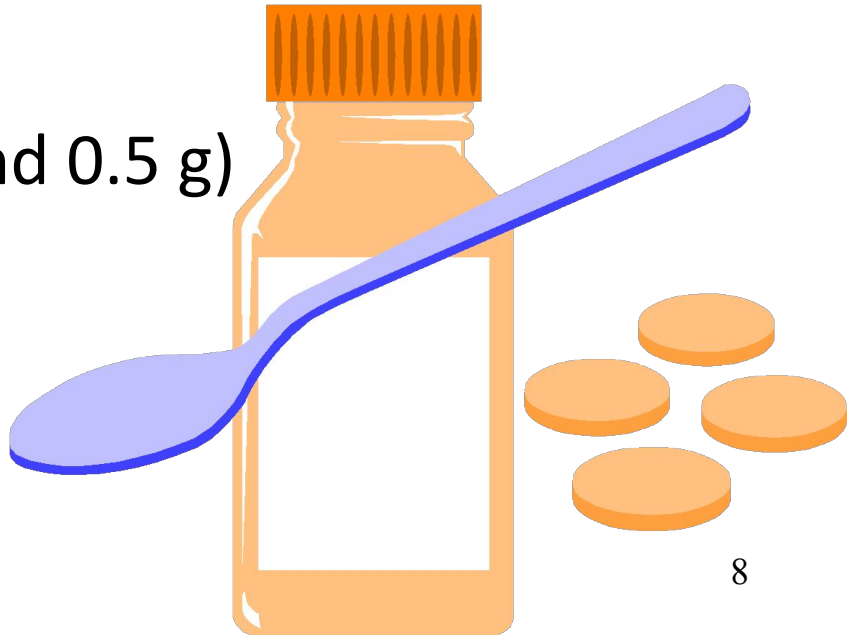
Fosfalugel

Calcium Carbonate (pulv. 0.25-1.0 g)

Magnesium Hydroxide (pulv. 0.25-1.0 g)

Magnesium Trisilicate

Sodium Bicarbonate (Tab. 0.3 and 0.5 g)



V. **Myogenic Spasmolytics**:

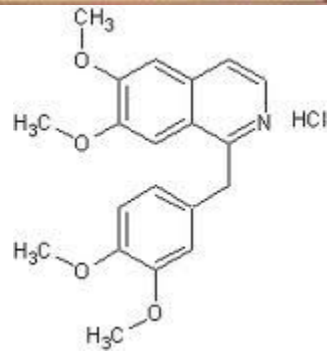
No-spa – amp. 2% solution -2 ml,

Tab. 0.04 g (40 mg)

Papaverine hydrochloride –

amp. 2% solution - 2 ml,

Tab. 0.04 g (40 mg)



VI. **Others**:

Solcoseryl (*amp. 2, 5 and 10 ml; vial 250 ml*)

H_2-antagonists Cimetidine, Ranitidine, Famotidine -

inhibit (by 90%) basal, food-stimulated, and

nocturnal secretion of gastric acid after a single dose.

They block **H_2-receptors** in the stomach, blood vessels, and other sites.

They are Competitive Antagonists of **Histamine** and

are fully reversible.

H_2-antagonists distribute widely throughout the body (including in breast milk and across the placenta) and

are excreted mainly in the urine.

Clinical Uses: Peptic Ulcers, Zollinger-Ellison Syndrome, Gastroesophageal Reflux Disease (heartburn)

Cimetidine has Endocrine effects and acts as a Nonsteroidal Antiandrogen

Endocrine effects:

Gynecomastia - abnormal overdevelopment of the breasts in a man

Galactorrhea - continuous release of milk

Impotence, Libido decrease, Reduced sperm count.

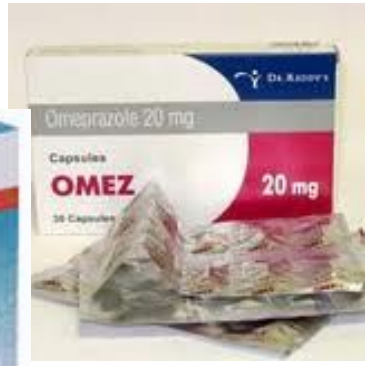
Cimetidine inhibits CYP-450 => Slows Metabolism => Potentiates the Action of some drugs:

- Warfarin
- Diazepam
- Phenytoin
- Quinidine
- Carbamazepine
- Theophylline
- Imipramine

OMEPRAZOLE is the prototype of substituted benzimidazoles, which inhibit the final step in gastric acid secretion and have overtaken H_2 blockers for acid-peptic disorders.

Mechanism of Action: Irreversible Inhibition of the H^+/K^+-ATPase (the Proton Pump) suppressing secretion of H^+ ions into the gastric lumen - the final step in the secretion of gastric acid.

It markedly inhibits both basal and stimulated gastric acid secretion.



daily dose Inhibits 100% of ic Acid secretion

Prostaglandins E_1 and E_2 :

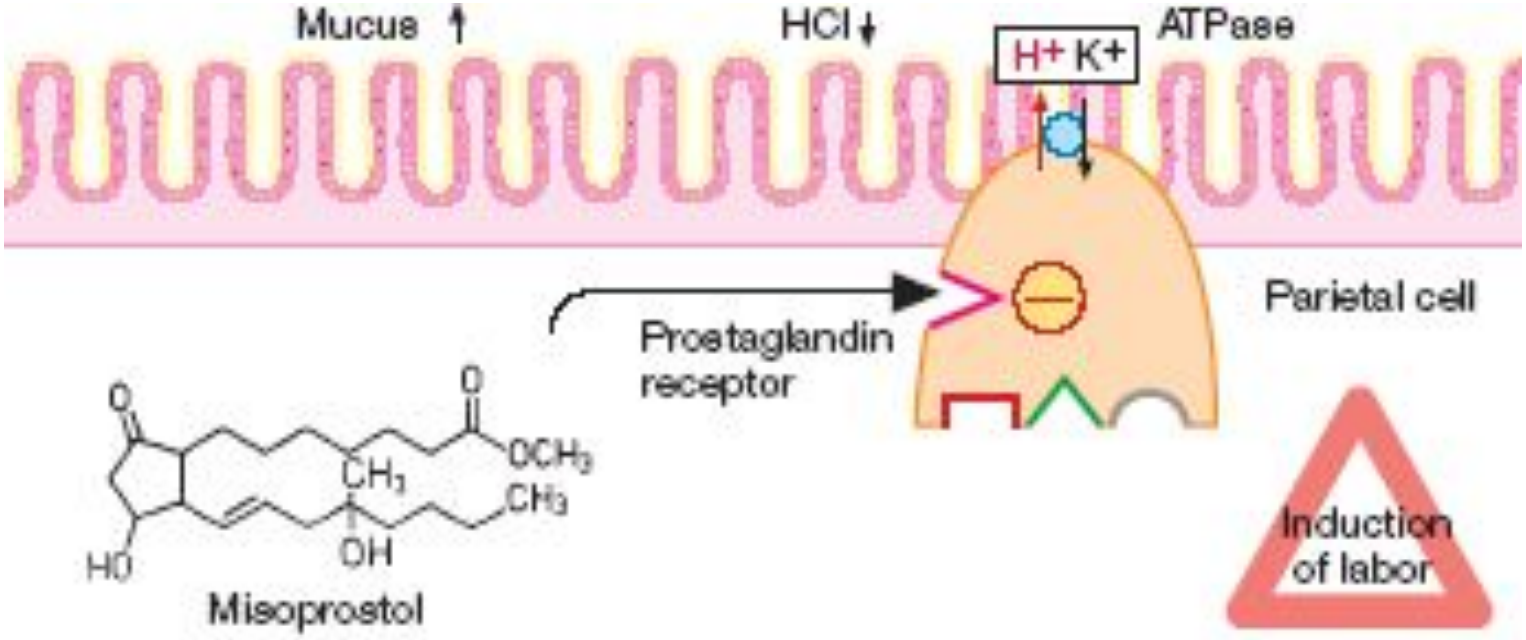
↓HCL and Gastric Acid Secretion

↑Secretion of mucus and bicarbonate

- CYTOPROTECTIVE EFFECT

MISOPROSTOL – a stable analog of PG E1

- is approved for prevention of gastric ulcers induced by NSAIDs



Chemical structure and protective effect of misoprostol

ANTACIDS are weak bases that react with gastric acid to form water and a salt, thereby diminishing gastric acidity.

Since PEPSIN is inactive at pH > 4.0,

Antacids also □PEPTIC ACTIVITY.

They ⇓ *Helicovacter Pylori* Colonization and

⇑ PGs synthesis.

Bismuth subnitrate [*Tab. «Vicairum», «Vicalinum»*]

De-nol [*Bismuth tripotassium dicitrate* – Tab. 0.12 g]

Aluminum hydroxide [*pulv. 0.25-1.0 g*]

Magnesium hydroxide [*pulv. 0.25-1.0 g*]

Almagel [*vial 170 ml*]

Maalox [*suspension 250 ml, chewable tab.*]

Sodium bicarbonate [*Tab. 0.3 and 0.5 g*]

Calcium carbonate [*pulv. 0.25-1.0 g*]

Emetic Agents - are the drugs that produce vomiting.
They may be classified as:

1. Centrally acting, by stimulation of the CTZ:

Apomorphine hydrochloride (*amp. 1%-1 ml*) -

a semisynthetic derivative of *Morphine*.

It stimulates D_2-receptors of the trigger zone.

Injected **SC**, it causes vomiting within 5 minutes

2. Peripherally acting: stimulate the *vomiting center* reflexively:

Preparations from *Thermopsis* and *Ipecacuanha*

Copper Sulfate and ***Zinc Sulfate*** have peripheral action through irritation of stomach mucosa.

Emesis has a reflexive character after their introduction, however they are not used to produce vomiting.

Antiemetic Agents

Metoclopramide – Tab. *5 mg*, amp. *0.5%-2 ml*

inhibits D_2 receptors in the brain's CTZ and

in high dose blocks 5-HT_3-receptors to inhibit or reduce nausea and vomiting.

Domperidone (*Motilium*) – Tab. 10 mg

- inhibits D_2 receptors.

Advantage of *Domperidone* is its no penetrating blood-brain barrier and no-inducing Extrapyramidal Effects.

<u>Clinical Uses</u>:

Functional disorders of the GIT,

Stomach hypotonia, Reflux-esophagitis.

Corticosteroids: Dexamethasone
Methylprednisolone
are effective against Emetogenic Chemotherapy.
Their antiemetic mechanism may involve blockade of PGs.

The antagonists of the Serotonin Receptors:

Ondansetron (amp. 0.2%- 2 and 4 ml, tab. 4 and 8 mg)

Tropisetron -

selectively block 5-HT_3 receptors:

- In the periphery (visceral afferent fibers) and
- In the brain (CTZ).

Ondansetron is approved for prevention of postoperative nausea and/or vomiting.

ANTIDIARRHEALS

Loperamide - is widely used to control acute and chronic diarrhea.

It is **phenylpiperidine** derivative and has Opioid-like actions on the gut:

Activates Presynaptic Opioid Receptors

in the enteric NS to inhibit Acetylcholine Release and decrease peristalsis.

Side effects: drowsiness, abdominal cramps, dizziness,

Toxic Megacolon => they should not be used in young children or patients with severe colitis.

Classification of Cholagogic Agents

I. Agents Stimulating Bile Formation:

1. **Agents Containing Bile Acids**: **Allochol**, **Cholenzyme**
2. **Synthetic agents**: **Oxaphenamide** (*tab. 0.25 g*)
3. **Plant drugs**: **Cholosas** (*vial 300 ml*)

II. Agents Stimulating Bile Migration:

1. **Cholekinetic agents** (increasing the **Bile Tone**):

   Magnesium Sulfate, **Sorbitol**, **Berberis**

2. **Cholespasmolytic agents** –

   Decreasing the Biliary Tract and **Sphincter Oddi tone**:

- **Spasmolytics**: **Papaverine, No-spa, Euphyllin, Magnesium Sulfate**
- **M-cholinoblockers**: **Platyphyllin hydrotartrate**

All **cholagogic agents** increase **bile production** by hepatic cells.

Cholosas (*vial 300 g*) is a syrup prepared from condensed **rosehip liquid extract** and sugar.

It is a dark brown syrup-like liquid the sour-sweet to taste.

Cholosas has choleretic action and stimulates bile formation.

Ripened Rose berries have a lot of **minerals** (*K, Ca, Mg, P, Fe, Cu, Mn, Cr, Mo, Co*) and **vitamins** (B_1, B_2, B_6, K, E, PP, C) tanning agents, carotin, riboflavin, citric and apple acids, phytoncides, essential oils.

Rosehip berries contain 5-10 times > of vitamin C than black currants and 40 times > than a lemon.

Water extraction methods allow to concentrate and preserve maximum of biologically active substances and the extract is **more potent** than raw berries.

Clinical uses:

cholecystitis, hepatitis, anemia, scurvy, kidney and bladder diseases.

Hepatoprotectors

Lipoic Acid [***Thioctic acid***]: Tab. 12 mg, amp. 0.5% - 2 ml

Legalon (*Silymarin*): Dr. 70 mg, Caps.140mg

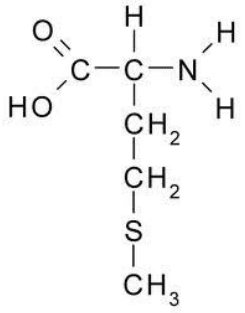
- contains Extract from **dry Lady's-milk** (*Silybum marianum*) and its flavonoids *Silymarin* and *Silybinin*.

Hepabene: 1 capsule contains 100 mg of **Lady's-milk** extract and 275 mg of **Fumitory** (*Fumaria officinalis*) extract.

=> **Cholagogic**, **Hepatoprotector** and **Spasmolytic** actions.

Methionine (essential amino acid)

PO 0.5 - 1.0 g 3-4 times / day



Clinical Uses:: Dyskinesia of Biliary Tracts, Toxic Liver Lesion, Alcoholism, Chronic Liver Diseases, Liver Cirrhosis.

Agents Used in Disturbances of the **Excretory Function** of **Pancreas**

I. **For Substitute Therapy:**

Pancreatin (***Creon***) contains **Pancreatic Enzymes**

Amylase, Protease, Lipase –

is extracted from **Fresh Hog Pancreas**.

Preparations containing ***Pancreatin***:

Digestal

Mezym-forte

Festal

Panzynorm

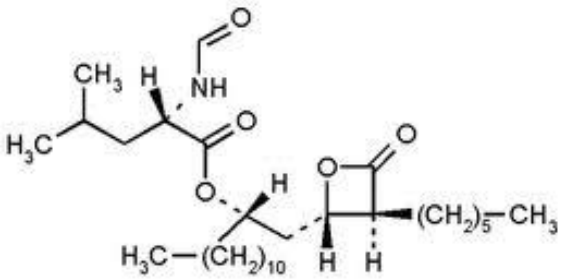
2. Inhibitors of the Proteolytic Enzymes of Pancreas

- are used mainly for patients with HYPERSECRETION of Pancreas at Acute Pancreatitis and as Systemic Haemostatic Agents.

CONTRICAL (*Trasylol, Aprotinin*) – vial *30 000 KIU/ml*
naturally occurring protease inhibitor.

- It inhibits Trypsin, Plasmin,
  and plasma and tissue Kallikreins.
- Inhibits Fibrinolysis through
  inhibition of *Plasmin* and *Kallikreins.*
- Inhibits activation of the Intrinsic Clotting System,
  a process that initiates coagulation and promotes fibrinolysis.

Orlistat is a pancreatic **Lipase inhibitor**, preventing the *breakdown* of **dietary fat** to **fatty acids** and **glycerols**.



It causes a **dose-related increase** in **fecal fat** that plateaus at 32% of dietary fat.

LAXATIVES

I. Irritant Laxatives – Purgatives, Cathartics

1. Small Bowel Irritant Purgative:

Vegetable oils: *Castor Oil* (*Oleum Ricini*)

2. Large Bowel Irritant Purgative:

- Drugs containing Antraglycosides:

Radix Rhei, Cortex Frangulae Alni, Folia Sennae

- Synthetic agents:

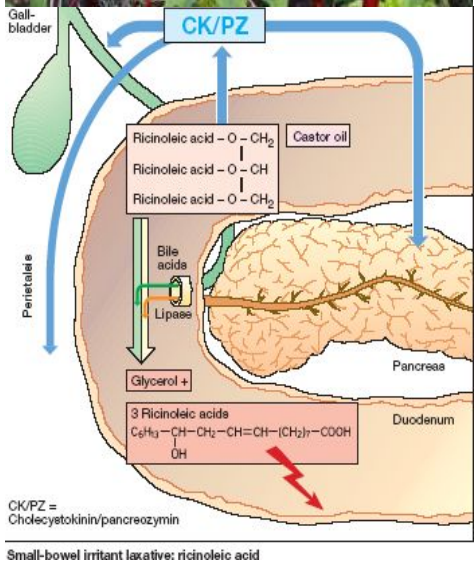
Phenolphthaleine, Isaphenine, BISACODYL

II. Osmotically Active Laxatives –

Agents acting on all Bowel Sections (Bulk Laxatives):

Salt laxatives: $MgSO_4$; Na_2SO_4

CASTOR OIL (*Oleum Ricini*) a small bowel irritant, is a colourless glutinous oil obtained from the seeds of the plant ***Ricinus communis*** and used as a cathartic and a fine lubricant.



Small-bowel irritant laxative: ricinoleic acid

When ingested, it is hydrolized in the intestine by pancreatic lipase to *glycerol* and *ricinoleic acid*.

Ricinoleic acid acts as an irritant and produces purgation.

As *ricinoleic* acid acts on the *small* intestine, It produces copious, liquid stools, with **fluid loss**.

It may stimulate uterine contraction in pregnant women.

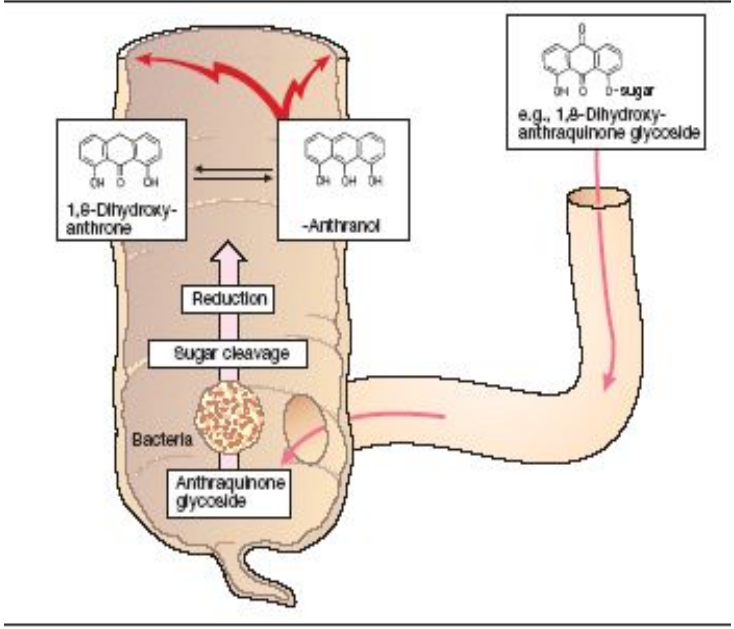
It can be employed after oral ingestion of a toxin to hasten elimination and to reduce absorption of toxin from the gut.

CASTOR OIL is not indicated after the ingestion of lipophilic toxins likely to depend on bile acids for their absorption.

LARGE BOWEL IRRITANT PURGATIVE

Drugs containing ANTRAGLYCOSIDES are of plant origin:

- Folia Sennae
- Ffructus Sennae -
  of the Senna plant

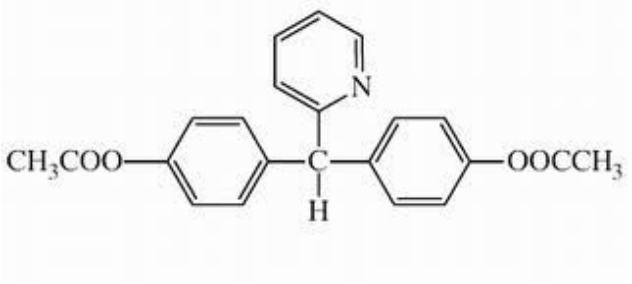


Large-bowel irritant laxatives: anthraquinone derivatives

- Cortex Frangulae – of the bark of Buckthorn
- Rhizoma Rhei - the roots of RHUBARB
- the Leaf Extract from Aloe Species.

Following ingestion of *galenical preparations* or of the *anthraglycosides*, discharge of soft stool occurs after a latency of 6 - 8 h.

The *anthraquinone glycosides* themselves are inactive but are converted by colon bacteria to the active free *aglycones*.



Bisacodyl (tab. 5 mg; rectal supp. 10 mg) is rapidly converted by intestinal enzymes and gut bacteria into its active metabolite which directly irritates and stimulates the large bowel.
Given by the enteral route, bisacodyl is subjected to hydrolysis of **acetyl residues**, absorption, conjugation in the liver to Glucuronic Acid (or also to sulfate), and biliary secretion into the duodenum.
Oral administration is followed by discharge of soft formed stool after 6-8 hours.
When given in suppository, it produces its effect within 1 h.

Thank You for Attention !