

**Ministry of Public Health of Ukraine
Higher State Educational Institution
"Ukrainian Medical Stomatological Academy"**

"Approved"

at a meeting of the Department of
Experimental and Clinical Pharmacology
with Clinical Immunology and Allergology

Head of the department

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**METHODICAL GUIDANCE FOR STUDENTS' SELF-DIRECTED
WORK WHEN PREPARING FOR PRACTICAL SESSION**

Academic subject	Clinical Pharmacology
Topic 5	The clinico-pharmacological characteristic the medicines, which influence the function of the digestive tract, hepatobiliary system and pancreas
Year of study	5
Faculty	Foreign students training (Medical)

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1. Relevance of theme:

At present treatment of ulcer disease with help M-cholinoblockers (nonselective drugs: *atropini sulfas*, *platyphyllini hydrotartras*, and *methacinum*, selective *M₁-Cholinoblockers*: *pirenzepinum* (*gastrocepinum*, *telenzepin*, and *H₂-histamine* receptor antagonists: *ranitidinum*), *famotidinum*), *nizatidinum*, and *roxatidinum*, proton pump inhibitors: *omeprazolum*, *lansoprazolum*, *pantoprazolum*, *rabeprazolum*, *esomeprazolum* allowed considerably to shorten the common number of surgical operations concerning ulcerous illness. In addition using of these preparations cause significant elongation of duration of remission in patients with ulcer disease. These preparations find also application for treatment of chronic hyperacid gastritis and syndrome Sollinger-Ellison. In the complex of therapy in ulcer disease, chronic hyperacid gastritis and syndrome Sollinger-Ellison are included drugs decreasing gastrointestinal activity (*motilium*, *metoclopramid*). Longlasting therapy with help these preparations may cause different side effects. In this connection the correction of complications of pharmacological therapy has the especially significant value. The account of possible side effects and toxic action of preparations helps to pick up correctly medication with account age of patient, concomitant pathology and other factors.

2. Learning objectives:

Student must capture skills of choice of safety of pharmacological therapy with help drugs acting on gastric secretion and motility of gastrointestinal tract;

Student must capture ability of forecast of the possible of side effects of drugs acting on gastric secretion and motility of gastrointestinal tract;

Student must be able to realize the correction of pharmacological therapy with help preparations of this group of medicinal agents if it necessary.

3. Basic knowledge, skills necessary for studying the subject (interdisciplinary integration)

Discipline	To know
Anatomy	Anatomic features of structure of organism of man (skeleton, vascular system, muscles).
Pathological physiology	Pathogenesis of infectious inflammatory process
Microbiology	Exciters which cause infectious-inflammatory diseases
Therapy, pediatrics, the surgery	Symptomatology, clinic of infectious process, diagnostics

4. Tasks for work during preparation for the classes.

4.1. The list of key terms, parameters, characteristics which the student is to assimilate while preparing for the class:

4.2. Theoretical questions for the class:

1. Name the antisecretory agents.
2. Name the drugs that are used to eradikatsiyi *Helicobacter pylori*.
3. Share Modern regimen of gastric ulcers and 12 duodenal ulcer.
4. Make a plan pharmacotherapy gastritis with increased secretion of the stomach.
5. Make a plan pharmacotherapy gastritis with reduced secretory function of the stomach.
6. Make a plan pharmacotherapy of irritable bowel syndrome.
7. Make a plan pharmacotherapy of chronic autoimmune hepatitis.
8. Make a plan pharmacotherapy of primary biliary cirrhosis.
9. Make a plan pharmacotherapy cirrhosis.
10. Make a plan for municipal economy pharmacotherapy.
11. Make a plan pharmacotherapy of chronic pancreatitis.

4.3. Practical tasks:

1. Make a plan pharmacotherapy of peptic ulcer disease 12 duodenal ulcer.
2. Make a plan pharmacotherapy gastritis.
3. Make a plan pharmacotherapy of gastric ulcers.
4. Master the skills of choosing effective and safe drug therapy drugs that affect the secretory-motor function of the gastrointestinal tract.
5. Master the skills of pharmacotherapy adjustment in the event of side effects.

Content topics

DRUGS ACTING ON GASTRIC SECRETION

DRUGS INCREASING GASTRIC SECRETION

These groups of drugs are divided into:

1. Diagnostic drugs — *pentagastrinum*,
2. Drugs of replacing therapy - *acidum hydrochloricum dilutum*, *pepsinum*, *succus gastricus naturalis* that indicate in hypoacidic, anacidic gastritis, achylia.

Polenzyme drugs such as *Pancreatinum*, *Festalum*, *Panzinorm forte*, *Mezymfork'* arc used when secretion

of stomach glands, pancreas, bile secretion are diminished.

DRUGS DECREASING GASTRIC SECRETION

Drugs that decrease gastric acid secretion are divided into:

1. M-Cholinoblockers;

1.1 Nonselective drugs: *atropini sulfas*, *platyphyllini hydrotartras*, and *methacinum*;

1.2 Selective *M₁-Cholinoblockers*: *pirenzepinum* (*gastrocepinum*);

2. H₂-histamine receptor antagonists: *ranitidinum* (*zantac*), *famotidinum* (*quamatelum*), *nizatidinum* (*axid*), and *roxatidinum*;

3. Proton pump inhibitors: *omeprazolum* (*Losec*, *Omez*), *lansoprazolum* (*Lancerol*), *pantoprazolum* (*Controlock*), *rabeprazolum* (*Pariet*), *esomeprazolum* (*Nexium*);

Antacids: *magnesii oxydum*, *natrii hydrocarbonas*, *Almagel*, *Maalox*, *Alumini hydroxidum*, *Rennie* etc.

H₂ Receptor Antagonists

The principal effect of H₂ receptor antagonists is to inhibit histamine-stimulated gastric acid secretion. They also inhibit gastric acid secretion induced by gastrin and acetylcholine.

Therapeutic uses: The major therapeutic use of H₂ receptor agonists is in the treatment of patients with duodenal and gastric ulcers and gastric hypersecretory states. The first drug was cimetidine that is not used now because of adverse effects: some degree of renal dysfunction, that resulted in the CNS disturbances (e.g. confusion), antiandrogenic effect, resulting in gynecomastia in men and galactorrhea in women, reduces liver blood flow and, thus, can markedly decrease the hepatic clearance of drugs whose metabolism is dependent on liver blood flow (e.g. *propranololum*). Because cimetidine reversibly inhibited the cytochrome P-450 hepatic enzyme system, a number of drug interactions are observed.

Ranitidinum is 4-12 times more potent than *cimetidinum*, and it is approved for the treatment of patients with gastroesophageal reflux disease. *Ranitidinum* does not significantly affect the cytochrome P-450 hepatic enzyme system, but it does reduce liver blood flow, have adverse CNS effects and drug interactions. The risk of untoward antiandrogenic effects from *ra-nitidinum* use appears to be minimal.

Famotidinum is most potent on a weight basis. Its efficacy in patients with peptic ulcer disease is similar to that of other agents. *Famotidinum* has a longer half-life than *cimetidinum* or *ranitidinum* (3 hours versus 2 hours). Pharmacodynamics and adverse reactions are similar to those of

ranitidinum.

Nizatidinum has the highest bioavailability and shortest half-life (1.6 hours) of the currently available H₂-receptor antagonists. *Nizatidinum*, like all of the currently available H₂-receptor antagonists, is principally excreted in the urine. Renal elimination involves both glomerular filtration and tubular secretion. Pharmacodynamics and adverse reactions are similar to those of *ranitidinum*

H⁺,K⁺-ATP-ASE INHIBITORS

Omeprazolum is the prototype of the benzimidazole sulfoxide prodrugs that diffuse across the gastric parietal cell cytoplasm, where they are pro-tonated. It binds to parietal cell H⁺, K⁺-ATP-ase, inhibiting secretion of hydrogen ions into the gastric lumen.

1. *Omeprazolum* is unstable in acid and is formulated in gelatin capsules. It is metabolized in the liver and excreted in the bile and urine.

2. By irreversibly inhibiting parietal cell H⁺, K⁺-ATPase and preventing the secretion of hydrogen ions into the gastric lumen, the drug appears to be more effective than *ranitidinum* for treatment of patients with gastroesophageal reflux. It has antihelicobacter effect.

3. *Omeprazolum* inhibits the oxidative metabolism of *phenytoinum*, *diazepamum*, and other drugs.

4. Although the incidence of adverse effects is low, toxicologic studies using high doses of *Omeprazolum* have demonstrated gastric carcinoid tumors in rats. Intense acid suppression leads to increased gastrin secretion, which has a trophic effect on gastric mucosa.

Other proton pump inhibitors have the same pharmacodynamics. *Rabeprazolum* is the most effective. *Esomeprazolum*, isomer of *Omeprazolum*, has better pharmacokinetics.

Antacides

Antacids interact with the HCL. Some of them are absorbed: *magnesii oxydum*, *natrii hydrocarbonas*, *calcii carbonas*, and *magnesii trisilicas*.

Natrii hydrocarbonas can cause systemic alkalization, sodium overload formation of heart increasing secretion. *Calcii carbonas* may induce hypercalciemia and reload increase of gastric secretions. *Magnesii oxydum* and *magnesii hydroxydum* may produce osmotic diarrhea and excessive absorption of magnesium in patients with renal failure may result in the CNS toxicity. *Alumini hydroxydum* is association with constipation. *Almagel*, *Maalox* and *aluminii hydroxydum* are not absorbed.

Gastroprotectors

Gastroprotectors are drugs increasing gastric and duodenal mucosa stability to aggressive factors of succus gastricus influence, they are divided:

1. Drugs increases mucosa defense function - *Misoprostolum* (*Saiotec*), *Carbenoxolum*, *Enprostolum*. *Misoprostolum* is a synthetic analogue of prostaglandinum E₂, stimulate mucosa, bicarbonates secretion, decreases HCL secretion. *Enprostolum* is a synthetic analogue of prostaglandinum E₂. *Carbenoxolum* is a drug of acidum glycyrrhizicum, stimulates mucosa and increases syalic acids content.

2. Drugs protecting mucosa mechanically *sucralfate (venter)*, *Bismuth tricalii dicitras* (De-Nol, Vis-Nol)
3. Complex drugs - *Vicalinum*, *Vicairum*.

Sucralfate is a complex substance formed from a sulfated disaccharide and polyaluminum hydroxide. It polymerizes when the pH falls below 4. The condensed polymer forms a gel, which adheres to the base of a duodenal ulcer crater. When *sucralfate* is administered before meals, it is effective for the treatment of patients with duodenal ulcer disease. Adverse reactions are minimal because it is not systemically absorbed.

CHOLERETIC DRUGS

Choleretic drugs stimulate bile secretion. They are divided into:

1. Drugs consist of bile acids - *cholenzymum*, *allocholum*, and *liobilum*,
2. Synthetic drugs - *oxaphenamidum*,
3. Plant drugs - *Cholosasum*, *Febicholum*, *Stylicum Stigmatis Zea Maydis*.

Cholecinetic drugs stimulate tonus of bile bladder - *magnesii sulfas*, and *sorbitolum*. **Cholespasmolytic drugs** have spasmolytic effect on biliary tract - *atropini sulfas*, *platyphyllini hydrotartras*, *papaverini hydrochloridum*, *nospanum*, and *magnesii sulfas*. **Cholelytolytic drugs** solve chole-steryne concrements in gall- bladder - *chenofalk*, *ursofalk*, *olimetinum*, and *urolesanum*. **Hepatoprotectors** increase stability of hepatocytes - *essencia-le*, *silimarinum*, *hepabene*, *thiotriazolinum*, *antralum*, *acidum lipoicum* etc.

Acidum lipoicum increases energy metabolism of hepatocytes. *Essenciale*, *silimarinum*, *hepatobene*, *thiotriazolinum*, *antralum* are antioxidants.

DRUGS USED IN PANCREATIC SECRETION DISORDERS

In chronic pancreatic secretory insufficiency enzymatic drugs (*pancre-atinum*, *festalum*, *pansinorm* etc) and spasmolytic drugs (*papaverini hydro-chloridum*, *drotaverinum*, *vinbaronum*) are used.

Proteolysis inhibitors decrease pancreas enzymes activity in the case of acute pancreatitis, pancreas cancer. Proteolysis inhibitors (*contrycalum*, *gordox*, *pantripinum*, *trasilolum*) inactivate trypsin circulating in blood, remove toxemia, block quinines, protect pancreas destruction and inhibit fibrinolysis.

Adverse effects: allergic reactions

Drug	Drug forms
Tinctura Absinthii	Flac. 25ml
Xenicalum	Caps. 0,12
Pancreatinum	Pulv.; Tab. 0,5
Panzinormum	Dragee
Contrykalum	30000 UA
Pentagastrinum	Amp. 0,025% - 2ml
Succus gastricus naturalis	Flac. 100ml
Pepsinum	Pulv.
Acidum hydrochloricum dilutum	Flac. 50ml
Ranitidinum	Tab. 0,15; Amp. 2,5% - 1ml
Famotidinum	Tab. 0,02, 0,04
Pirenzepinum	Tab. 0,025; Amp. 0,01
Omeprazolum	Caps. 0,02
Natrii hydrocarbonas	Pulv.; Tab. 0,3, 0,5
Almagelum	Flac. 150ml
Maalox	Tab.; Flac. 15ml
De-nolum	Caps. 0,12
Аротофбіпит hydrochloridum	Amp. 1% 1ml
Aethaperazinum	Tab. 0,004, 0,006, 0,01
Metoclopramidum	Tab. 0,01; Amp. 0,5% - 2ml
Allocholum	Tab.
Cholenzymum	Tab.
Cholosasum	Flac. 300ml
Cholagolum	Flac. 10ml
Oxaphenamidum	Tab. 0,25
Magnesii sulfas	Pulv.

Essentiale Forte	Caps.; Amp. 5ml
Siliborum	Tab. 0,04
Darsilum	Tab.
Oleum Ricini	Flac. 30, 50ml; Caps. 1,0
Bisacodylum	Dragee 0,005; Supp. rect. 0,01
Senadexinum	Tab.
Loperamidi hydrochloridum	Tab. 0,002
Hylacum	Flac. 30, 100ml
Bactisubtilum	Caps.

Materials for self-control

A. Test for self-control

1. An increase in gastric acid secretion results from stimulation of the following gastric mucosal receptors?

- a) histamine H₁- receptors
- b) histamine H₂- receptors
- c) M₁-cholinoreceptors
- d) M₂-cholinoreceptors
- e) β-adrenoreceptors

2. Ranitidine causes effective inhibitions of gastric secretion induced by

- a) Histamine
- b) Pentagastrin
- c) Methacholine
- d) Aspirin
- e) Vagal stimulation

3. Cimetidine can prolong the action of ...

- a) Phenytoin
- b) Diazepam
- c) Propranolol
- d) Imipramine
- e) Pirenzepine

4. Which of the following drugs are known as gastroprotectors due to their ability to increase mucus and bicarbonate secretion?

- a) Carbenoxolone
- b) Pirenzepine
- c) Omeprazole
- d) Misoprostol
- e) Bismuth subcitrate

5. Name the following mechanisms responsible for the ulcerhealing effect of bismuth compounds

- a) acid neutralisation
- b) increase in prostaglandin synthesis
- c) inhibition of Helicobacter pylori
- d) inhibition of M-cholinoreceptor
- e) inhibition of gastroduodenal motility

6. Which of the following statements pertaining to pirenzepine are true?

- a) It is a selective antagonist of cholinergic muscarinic M₂ receptors
- b) It does not produce blurred vision and dry mouth
- c) It increases gastric bicarbonate secretion
- d) Gastric secretion is not affected
- e) Gastric secretion is not affected
- f) Gastric acid secretion is reduced

7. Which of these laxatives are used to remove the poison from intestine?

- a) Sodium phosphate
- b) Liquid paraffin
- c) Sorbitol
- d) Magnesium sulfate
- e) Phenolphthalein

8) Which of the following drugs are used for treatment of gastroesophageal reflux?

- a) Cimetidine
- b) Pimozole
- c) Hyoscine
- d) Ondansetron

9) The anti-emetic with specific clinical use in motion sickness as well as Ménière's syndrome are

- a) Cinnarizine
- b) Cimetidine
- c) Hyoscine
- d) Chlorpromazine
- e) Metoclopramide

10. Which one of the following drugs prevents activation of proteolytic enzymes in pancreatic gland

- a) Pancreatin
- b) Festal
- c) Contrycal
- d) Papain
- e) Panzynom

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