

**FORMATION OF MEDICAL OUTLOOK OF FIRST-YEAR STUDENTS ON
THE EXAMPLE OF STUDYING KINETICS IN THE DISCIPLINE
“MEDICAL CHEMISTRY”**

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When considering the section on the kinetic laws of processes, we think it is advisable to start with an understanding of such important concepts as chemical reaction: homogeneous and heterogeneous; molecularity (mono-, bi-, tri-); reaction order (zero, first, second order); half-transformation period; elimination half-life; examples. Having a certain basis, we then determine the rate of homogeneous and heterogeneous reactions and determine on which factors the rate depends, namely on the concentration of the reacting substances under given external conditions (we consider the law of active masses by K. Gulberg and P. Vaage); on temperature (we consider the Van't Hoff's rule); on activation energy (we consider the theory of active collisions by S. M. Arrhenius); on the presence of positive and negative catalysts (we consider catalysis, autocatalysis, promoters); on the aggregate composition of the catalyst and reactants (we distinguish between homogeneous and heterogeneous catalysis, microheterogeneous catalysis).

We place special emphasis on multiplet, electronic-chemical theory, theory of active ensembles. We consider acid-base catalysis to be one of the interesting issues of the topic. And then we proceed to consider the kinetics of enzymatic reactions - we characterize enzymes (simple and complex) as biological catalysts, compare their activation energy with the activation energy of ordinary non-biological catalysts,

explain the peculiarities, and also explain how the names of enzymes are formed: oxyreductases, hydrolases, transferases, lyases, isomerases, ligases. Such properties of enzymes as high efficiency, specificity (absolute and relative group), mild conditions for the course of reactions, a certain temperature regime and the optimum of enzymatic activity within the pH range are of interest to students of education.

We place special attention on the kinetics of enzymatic reactions, considering the theory of E. Fischer (enzyme : substrate = key : lock), the Michaelis-Menten theory (dependence of the initial rate of the enzymatic reaction on the substrate concentration). Our students are interested in the question “Contribution of domestic scientists to the study of catalysis” - we focus the attention of first-year students on the fact that we have people to be proud of, tell them about L. V. Pisarzhevsky, G. I. Golodets, V. A. Rojter, M. V. Polyakov and others. Students are also interested in the mechanisms and kinetic features of complex chemical processes: sequential, parallel, reversible, combined (especially conjugated, which play a special role in chemistry and biology), chain, and cyclic. We provide a huge number of specific examples that are understandable and that are liked by students.

Considering the questions of the kinetics of chemical and biochemical reactions in the study of the educational component “Medical Chemistry”, we consider it expedient to tell the first-year students of the specialty “Medicine” about:

1) pharmacokinetics - we focus on the fact that the introduction, absorption, absorption of drugs in the patient's body, and then their removal from the body are interrelated processes that depend on the ability of drug molecules to overcome various barriers that are saturated in living organisms: One example is membrane phospholipids, and drugs can overcome them through the following mechanisms: passive diffusion, facilitated diffusion with the help of carrier agents, as well as filtration and active transport;

2) some pharmacokinetic parameters (the rate constant of drug distribution in the body [parameter α] and the rate constant of terminal elimination [parameter β] - this parameter corresponds to the terminal half-life of the drug from the body).

When considering the subject “Diffusion”, we draw attention of students to the

fact that the process of distribution of molecules of one substance among the molecules of another, i.e. “diffusion”, is one of the main ways by which a drug penetrates the patient's body: Fick's law describes the rate of diffusion of a substance in the direction of its concentration gradient. We are sure to give examples, namely passive diffusion, diffusion in the aqueous phase, and diffusion during ionization. When considering the diffusion of ionization, we pay special attention to the fact that most drugs are complex organic bases or acids that are electrolytes and therefore the degree of their ionization depends on the pH of the environment in which they are contained. In this regard, we remind students of the Henderson-Hasselbach equation for a weak acid or base, which was studied in the subject “Solutions. Acid-base equilibrium. Buffer systems”. We pay attention to the relationship between the pH of the medium, the dissociation constant, and the degree of ionization:

$$\text{pH} = \text{pK}_a \pm \lg \frac{\alpha}{1 - \alpha}$$

(«+» - corresponds to acid; a «- » - corresponds to base).

When discussing this subject, we remind first-year students that an important characteristic of weak acids and weak bases is ionization, explaining that such drugs are ionized to a certain extent in the environments in which they enter the patient's body. It is important to understand the degree of ionization of the drug in a particular environment from which it is absorbed in the patient's body and distributed to organs and tissues. We draw attention to the fact that in some cases the non-ionized part of the drug is well soluble in lipids, better penetrates through cell membranes. The degree of ionization depends on the pH of the medium and the pK of the drug (pK_d). It is the pH of the medium and the pK_d that make it possible to determine the ratio of the ionized concentration of the drug (C_i) to the unionized concentration (C_{un}). This is the Henderson-Hasselbach equation for drugs that are weak acids:

$$\lg (C_i/C_{un}) = \text{pH} - \text{pK}_a$$

b) that are weak bases:

$$\lg (C_{un}/C_i) = \text{pH} - \text{pK}_a .$$

Considering the pharmacokinetics of chemical reactions, we draw the attention of students to the fact that pH and changes in this value affect the rate of diffusion

(including through membrane barriers) and elimination. We consider it appropriate to give examples: if the drug is prescribed orally (per os - through the oral cavity (lat.)), then it moves through various medium with a certain pH value, namely through the stomach ($\text{pH} \approx 1.0$), the upper parts of the small intestine ($\text{pH} \approx 6.8$), lower parts of the small intestine ($\text{pH} \approx 7.6$). We explain to first-year students that if $\text{pH} = \text{pKa}$ (since the percentage of ionized drug molecules is related to pH and pKa), then 50% of the drug is in soluble form, and the other 50% is insoluble (in lipid). Thus, aspirin (acetylsalicylic acid - ASA) with $\text{pKa} = 3.5$ - with an increase in pH will be more ionized and will be less soluble in lipids, therefore acidic drugs are better absorbed in the stomach than in the intestines.

It is known that the pH of urine is from 4.6 to 8.2, which makes it possible to regulate both passive diffusion and reabsorption of drugs. Thus, alkalization of urine can lead to a significant increase in the elimination of acidic compounds by the kidneys, including ASA. A change in the pH of the medium affects the diffusion of drugs through membrane barriers.

Thus, the excretion of salicylic acid (a metabolite of ASA) increases with urine alkalization, which is explained by the fact that it is in an ionized form (sodium salt), which is poorly soluble in lipids. Considering the issues of kinetics, we are preparing the basis for Pharmacology, which students will study in the third year, but today we still pay attention to the Michaelis-Menten equation, namely, that the rate of the kinetic process described in this equation allows us to calculate the rate at which a drug is transported at a certain concentration, and we also focus on the Michaelis constant, which characterizes the concentration of a drug that corresponds to 50% of the maximum rate at which the kinetic process occurs.

Thus, we considered certain issues of the kinetics of chemical and biochemical reactions, including pharmacokinetics, which we consider appropriate to consider with students when studying the educational component "Medical Chemistry" in order to create a medical worldview in first-year students and to improve their perception of educational material when studying educational components of "Biological Chemistry" and "Pharmacology" in the second and third years.

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