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Medical chemistry

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Fifth edition,
corrected

Approved
by the Ministry of Education and Science
of Ukraine as a textbook for students
of higher education establishments —
medical universities, institutes, and
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Published in accordance with the Order
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The textbook outlines the fundamentals of bioenergetics and cybernetics of biochemical reactions; describes the properties of solutions and their role in biochemical processes; presents modern concepts of electrode processes; explains peculiarities of surface phenomena and their value for the vital activity of the body; dwells on the properties of dispersion systems and biopolymer solutions. Special emphasis is placed on biogenic elements and their properties viewed through the spectacle of modern concepts of atomic and molecular structure, and chemical bonds.

The authors touch upon topical problems of ecology.

The textbook is intended for English-speaking students of higher education establishments — medical universities, institutes, and academies, pharmaceutical, biological, and ecological specialties.

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Contents

PREFACE

In their deep sense chemistry and medicine are inseparable.
M. Lomonosov

The 20th century is marked by considerable changes in the field of techniques of chemical and physicochemical investigations, practical application of new chemical disciplines including medical chemistry.

Medical chemistry studies the chemical basis of the vital activity processes of the organism, which are explained on the ground of theoretical foundation of inorganic, physical and colloid chemistry. For example, changes of the structure and functions of blood cells in blood substitute solutions are explained by osmotic pressure laws, electrolyte ion distribution between cells and external medium – by laws of Donnan membrane equilibrium, the mechanism of nervous impulse transmission – by the electrolytic dissociation theory, the constancy of H^+ ions in biological liquids to a considerable extend depends on the presence of buffer systems in their composition. The theory of oxidation-reduction potentials allows understanding the proceeding of many reactions in the human body conditioned by energy intake and expenditure. Features of the physical chemistry of surface phenomena help to interpret drug action mechanism, explain the phenomena of phagocytosis and immunity.

The kinetics and catalysis theory gives a possibility to understand the laws of enzymatic and pharmacokinetic processes proceeding. Theoretical tenets of colloidal chemistry help to understand the role of the factors of human body disperse systems stability in the process of vital activity.

Medical chemistry studies the structure and reactivity of the most important biologically active molecules, the theory of chemical bond in complex compounds formed by biological metals and biological ligands, and the importance of biogenic elements in the vital activity of the organism. It studies the processes on molecular and submolecular levels, since that is where one should look for causes of different diseases and hereditary characters. The knowledge of chemistry laws gives a possibility to influence purposively the metabolism of a sick organism.

No science has opened and done for man so much as chemistry. Recently chemistry has provided the humanity with numerous basic commodities and luxury items, which have improved the quality of life, gave a possibility to live in cleanness and receive high quality treatment.

The progress of modern medicine has been caused by achievements in chemistry to a large extent. The positive effect of medical activity is by 70 % conditioned by availability of drugs, the majority of which has been synthesized by chemists.

Successful introduction of computers has given a possibility to develop programs foreseeing which of new chemical structures may be especially effective in pharmacological application.

At present in practical medicine the techniques based on the theoretical evidence of physical and colloid chemistry are widely used (for diagnostics and treatment). These include hemodialysis, hemosorption, hemofiltration, preparative electrophoresis of cells, etc.

Medical chemistry provides with versatile information such disciplines as biochemistry, physiology, bioorganic chemistry, pharmacology, medical and biological physics, hygiene, toxicology, therapy, anesthesiology, physiotherapy, etc.

In their turn these disciplines as a primary information source have to influence the development of medical chemistry.

Wide application of chemistry in medicine emphasizes the wisdom of the thought of the Kyiv-Mohyla academy graduate, great Russian scientist M. Lomonosov: «... a medical man is not perfect without sufficient cognition of chemistry.»

Chapter 1

CHEMICAL BONDING AND COMPLEXING

Science has its own temples, each built through the efforts of several architects and numerous workers.
G. Lewis

When basses, which are absolutery ruling the world, suddenly fall silent in music, it makes an impression that the evil spirit has disappeared. What seemed uncontrollable is now ordered as if by magic.
L. Boltzmann

After studying this chapter you will be able to:

- classify chemical bonds;
- use experimental characteristics of chemical bonds;
- explain the ways of covalent bond formation;
- estimate the valency, coordination number, oxidation number of atoms in molecules; distinguish polar and nonpolar covalent bonds;
- explain the influence of hydrogen bonding on physical and chemical properties of substances;
- differentiate coordination compounds from other compounds;
- analyze the composition and structure of complexes; classify them;
- give examples of complexon application in medicine and explain the mechanism of complexons acting as antidotes.

1.1. Chemical bond and its experimental characteristics

The basic condition of chemical bond formation is diminution of the total energy of the polyatomic system in comparison with the energy of isolated atoms.

The chemical bond nature according to modern ideas is explained by the interaction of electric fields formed by electrons and atomic nucleuses that take part in chemical compound formation.

Depending on the character of electronic density distribution between interacting atoms covalent, ionic, and metallic bonds are distinguished.

Bond length, strength and valency angles are the basic parameters of chemical bonds defined by physical methods.

Bond length is a distance between the nucleuses of the atoms forming a chemical bond.

The unit of bond length measurement is the nanometer (1 nm = 10^{-9} m) or angstrom (1Å = 10^{-10} m).

Energy should be spent to rupture a bond.

Bond strength is determined by the minimum energy required for rupturing chemical bonds in 1 mol of a substance to obtain isolated atoms.

The unit of bond strength measurement is kJ/mol.

The angle between conditional straight lines passing through the nucleuses of chemically combined atoms is called the valency angle.

The unit of valency angle measurement is the degree. For example, for a molecule of water the bond length of H—O is 0.096 nm, bond energy is 464 kJ/mol, and the angle between the H—O—H bond is 104.5°.

1.2. Covalent bond

A covalent bond is a chemical bond between two atoms arising due to a shared electron pair.

Formation of a hydrogen molecule H_2 from separate atoms may be one of the simplest examples of covalent bond formation. When isolated atoms having electrons with opposite spins approach each other, they are attracted to each other. As a result their electronic clouds (atomic orbitals) are overlapped, and the highest electron density is located in the space between the nucleuses.

Schematically formation of a H_2 molecule can be represented as:

$$H\cdot + \cdot H \rightarrow H:H.$$

Valence electrons are marked on the scheme by points near the symbol of the chemical element. A shared pair of electrons may be indicated with a hyphen: H–H.

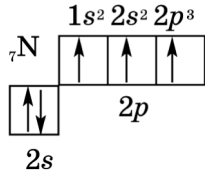
This method of molecule description is called the ***valence bond method***. More detailed fundamental tenets may be formulated in the following way:

1) a covalent bond is formed by two atoms at the expense of two electrons with antiparallel spins, which means a chemical bond is localized between two atoms;

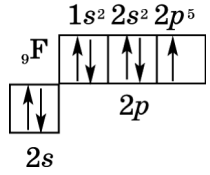
2) a covalent bond is situated in the direction where the strongest bonds are formed, i.e. where the approachment of atoms occurs by means of maximum overlapping between the atomic orbitals;

3) the strength of a covalent bond is larger if overlapping of electronic clouds is fuller.

Ways of covalent bond formation. Location of two electrons in the action field of two nucleuses is energetically more advantageous than staying of such electrons in the field of their own nucleuses, therefore all one-electron orbitals of the external energy level take part in the formation of a covalent bond. For example, the nitrogen atom has three unpaired electrons in the outer shell:

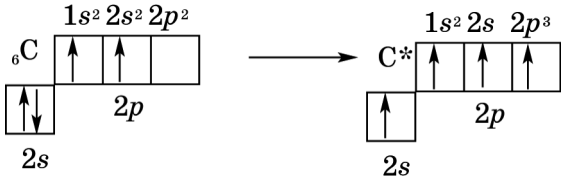


And the fluorine atom has one electron in the outer shell:



Thus these atoms can form respectively three bonds and one bond at the expense of unpaired electrons: N≡N; F—F.

The number of unpaired electrons can increase if an atom transits from a normal to an excited state at the expense of electron «steaming»:



In this case the atom is capable to form a greater number of bonds. «Steaming» of electrons requires energy expenses that are reduced in bond formation, but, as