MEDICAL UNIVERSITY – SOFIA

FACULTY OF DENTAL MEDECINE

CURRICULUM

Name of the course: ***Medical Chemistry***

Education degree: ***Master***

Type of the course: ***Compulsory education***
(Compulsory, elective, facultative)

Duration of the course: ***One semester, First semester***

Level of the course: **Level M /master level/**

Forms of evaluation: ***Current evaluations, seminars, tests, colloquium, practical exam***

Forms of education - **Lectures, seminars, discussion**

Semestrial exam: **Yes**

Lecturers: Assoc. prof. Ivan Ivanov
Assoc. prof. Cyril Naidenov

Department of **Medical chemistry and biochemistry**

ANNOTATION OF COURSE:

The course in medical chemistry allows dental students to acquire basic knowledge and competence in the field of chemistry, necessary for their careers. **The main directions are:**
1. To acquire theoretical and practical knowledge of chemical methods of analysis;
2. To acquire knowledge necessary to solve issues related to dental practice such as:
- Redox processes, redox potential and galvanic element in the oral cavity;
- Nature of corrosion processes and methods to prevent them;
- Selection of appropriate methods for analysis and proof of ions;
- Preparation of solutions with known concentrations;
- Calculation and experimental determination of the pH of solutions of acids and bases; pH measurements in biological materials;
- Preparation of buffer solutions used in dental practice.

3. To acquire knowledge of basic chemical compounds involved in the biochemical processes of the living organisms as amino acids, carbohydrates, lipids, heterocyclic compounds, nucleic acids, vitamins, hormones, etc.
4. To analyze the relationship between chemical structure of organic compounds, drugs and their biological activity.

DESCRIPTION OF THE COURSE:

The course consists of 75 academic hours, including:
• Lectures - 45 hours
• Practical exercises - 30 hours
(Laboratory exercises, seminars, colloquium).

The evaluation of the students comprises:

• Continuous assessment, by which the students are evaluated for their activity during the course;
• Practical test;
• Written exam.

Aspects of formation of the evaluation:

• Skills in solving the experimental tasks;
• Tests;
• Participation in discussions and colloquium;
• Practical exam
• Examination results during the session.

AUXILIARY MEANS FOR TEACHING:

schemes, molecular models, presentations, laboratory equipment and apparatuses.

PURPOSE OF THE CURRICULUM:

Asquisition of theoretical and practical skills in:

• peparation of solutions with a known concentration;
• determination of the pH of the solutions and in biological fluids;
• preparation of buffer solutions with desired pH;
• analysis of solutions containing different ions;
• reactions associated with complex formation;

• processes associated with polymerization and polycondensation;
• studying the properties of the main types of organic compounds in accordance with modern dental requirements.

TASKS OF THE PROGRAMME:

• Practical skills in analysis of biologically important substances using modern analytical and physicochemical methods of analysis;
• Solving of practical problems associated with the preparation and use of various concentrations, pH, buffers, surfactants;
• Analysis of various ions, biologically important organic compounds, vitamins, medicines, etc.

Prerequisites:

To start training of Medical Chemistry is necessary for the students to have basic knowledge of inorganic and organic chemistry, which is verified by the candidate student exam in chemistry.

EXPECTED RESULTS:

After completion of the course students should be able to:
• analyze inorganic and organic substances used in dental practice;
• know well the redox processes, and hence the processes associated with corrosion of dental materials and ways of preventing them;
• solve experimental tasks related to preparation of solutions with specific concentrations and use the different concentrations by passing from one to another;
• determine the pH in biological materials;
• prepare buffers with defined pH;
• know the properties of different types of surface-active substances and the use of non-ionic surfactant in the prevention of tartar;
• make the connection between the structure of the used materials in dentistry and their biological action.

Topics for independent work:

Set up essays or presentations on certain topics.

Literature:

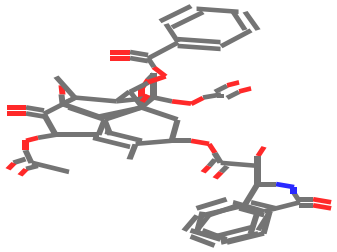
1. *Medical chemistry. Theoretical course for students.* M. Nikolov, Iv. Ivanov, M.Matova, R.Tomova, Ts.Tsanova. Medical University, Sofia“, Publishing House, Pedagog 6”, Sofia, 2011.
2. *Practical Course of Chemistry for English speaking students.* The authors are from the Department of Medical Chemistry&Biochemistry, Faculty of Medicine, Medical University, Sofia, Published by “Reko”, Sofia 2009.

Synopsis for the exam: see Annex

Medical University- Sofia
F a c u l t y of M e d i c i n e
Department of Medical Chemistry and Biochemistry

SYNOPSIS
of Medical Chemistry

for English-Speaking Students from the Faculty of Dental Medicine



I. GENERAL AND I N O R G A N I C C H E M I S T R Y

Theoretical Bases of Medical Chemistry

1. Bonding. Ionic and covalent bonds

1.1. Nature of chemical bonding. Method of valence bonds. Types of covalent bonds: σ–, π– and δ–bonds. Properties of the covalent bond. Delocalization of the chemical bond. Hybridization of the atom orbitals.

1.2. Nature of hydrogen bond and biological significants. Intramolecular and inter-molecular hydrogen bonds. Role of hydrogen bond for the stability and formation of biological structures. Intermolecular (ion-dipole forces, dipole-dipole forces, London dispersion forces) and ionic forces of attraction and their biological role. Metal bond.

1.3. Chemical bonds in complex compounds. Donor-acceptor (coordinative) bond. Classification and nomenclature of the complex compounds. Isomerism, structure and stability of complex compounds. Chelates in living systems. Application of certain chelates in dental practice.

1.4. Chemical bonds and electronic effects in molecules of organic compounds. Inductive and resonance (mesomeric) effects. Relationship between electronic structure and chemical properties.

2. Dispersed systems:

2.1. Solutions and solubility. Saturated solutions of low soluble ionic compounds in water - solubility product constant. Units of concentration.

2.2. Weak electrolytes. Equilibrium in electrolyte solutions. Dissociation constant. Degree of dissociation. Ostwald's dilution law. Theory of strong electrolytes – activity and ionic strength.

2.3. Colligative properties of solutions: vapour pressure lowering, boiling point elevation, freezing point depression. Raoult's laws. Osmosis and osmotic pressure. Biological significance.
2.4. Acid-base systems. Protolysis processes: Broensted-Lowry's conceptions of acids and bases. Conjugate acid-base pair. Acid-base strength – acid ionization constant (K_a) and base ionization constant (K_b). Lewis acids - bases.
2.5. Hydrolysis processes. The degree of hydrolysis and hydrolysis constant. Types of hydrolysis. Hydrolyses of organic compounds. Significance of hydrolysis processes.
2.6. Ionization of water. Ion product constant of water. The pH-scale. Physiological pH values. Methods for calculations and measuring the pH of solutions.
2.7. Buffer solutions-properties.The Henderson-Hesselbach equation. Buffer capacity. Blood's buffers. Buffer solutions used in dental practice.
2.8. Colloid dispersed systems. Classification of colloid dispersed systems. Methods of obtaining. Dialysis. Structure of the hydrophobic colloid particles. Kinetic, optical and electric properties. Electrophoresis. Solutions of high–molecular compounds. Stability and coagulation of colloid solutions. Biological significance. Reversible and irreversible hydrocolloids (alginates) used as elastic impression materials in dentistry

3. Chemical kinetics and chemical equilibrium

3.1. Chemical reaction rate. Dependence of reaction rate on concentration of reactants. Rate law. Rate constant. Reaction order. Rate equations of different reaction order.
3.2. Effect of temperature on the rate of chemical reactions. A reaction energy diagram. Transition state. Activation energy and the Arrhenius equation.
3.2. Catalysis. Theory of catalytic processes in point of view of transitional state. Mechanism of homogeneous and heterogeneous catalysis. Role of the catalysts in vital processes - biocatalysis.
3.3. Criteria for determination of direction of chemical processes and principles thermodynamics quantities: enthalpy, entropy and free energy. Spontaneity of chemical reactions and free energy. Exergonic, endergonic and anergonic processes. Conjugated processes. Compounds with macroergic bonds. Anergonic processes in living organisms.
3.4. Chemical equilibrium. The concept of equilibrium: The forward and the reverse reaction. The equilibrium constant and change in free energy (reaction isotherm of van't Hoff). Factors affecting equilibrium. Le Châtelier's principle and chemical equilibrium.

4. Processes of electron transfer

4.1. Valency and oxidation number. Reactions of oxidation and reduction. Electron exchange and types of redox processes.
4.2. Galvanic cell of Daniell. Galvanic cell in the oral cavity. Electrode half reactions. Electrode potential. Electromotive force of galvanic element. Nernst's equation. Direction of redox processes. Relationship between redox - potential and equilibrium constant. Redox systems in living organisms. Characteristics of biological oxidation.
4.3. Corrosion. Types of corrosion. Biochemical corrosion. Nature of the electrochemical corrosion. Oral electrogalvanic element in cases of bimetallism and polymetallism. Methods for prevention of corrosion.

5. Surface phenomena

Adsorption. Surface energy and surface tension. Adsorption on the surface: liquid/gas; liquid/liquid; liquid/solid substance. Adsorption equilibrium. Adsorption isotherm. The Langmuir equation. Ion exchange and selective adsorption. Lyotropic series. Surface-active substances and their use in dentistry. Chromatography - nature, types and application.

II. O R G A N I C C H E M I S T R Y

1.Hydrocarbons.

1 . 1 Saturated hydrocarbons. The reactivity of **alkanes and cycloalkanes.** Halogenation of alkanes - mechanism of reactions of free radical substitution (S_R). Free radicals and cancerogenese. **Cyclohexane** – conformation "chair" and "boat".

1.2. **Unsaturated hydrocarbons. Alkenes and alkynes:** structure and properties. Stereoisomerism: geometrical (*cis* - *trans*) isomerism. Acidity of alkynes. Mechanism of electrophilic addition to double bond (A_E). Oxidation, reduction and polymerization of alkenes and alkynes. Mechanism of polymerization. Plastics as the most used dental materials.

1.3. **Aromatic hydrocarbons**. Hueckel's rule of aromaticity. Mechanism of electrophilic aromatic substitution (S_E). Activators and deactivators. Orientation in benzene ring. **Fused aromatic hydrocarbons.** Carcinogens.

2. Hydroxyl derivatives of hydrocarbons and thiols.

Structures and chemical properties of alcohols and phenols. Alcohols as acids and bases. Acidity of phenols. Mechanism of esterification. Bio-oxidation of methanol, ethanol and glycol. Mercaptans (thioalcohols), thioethers: physical and chemical properties. Oxidation. Mercaptans (thioplastic materials) used as impression materials in dentistry.

3. Carbonyl compounds. Aldehydes and ketones.

Reactivity and comparative review of chemical properties of aldehydes and ketones: nucleophilic addition (A_N), oxidation and reduction. Important aldehydes and ketones. Reactions of polymerization and polycondenzation. Aldol condensation and its role in the biological processes. Cannizzaro's reaction. Use of some carbonyl compounds in dental practice. Quinones-structure and properties. Phylloquinone (vitamin K_1).

4. Carboxylic acids.

4.1. **Saturated monocarboxylic fatty acids and aromatic monocarboxylic acids.** Important representatives: formic acid, acetic acid, propionic acid, butyric acid, valeric acid (pentanoic acid) and benzoic acid. Chemical properties. Relationship between structure and acidity.

4.2.**Unsaturated monocarboxylic fatty acids:** chemical properties and representatives: acrylic acid, methacrylic acid and oleic acid. Polyunsaturated essential fatty acids: linoleic, linolenic and arachidonic, eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids (Vitamin F). Role of polyunsaturated ω–3 fatty acids for prevention of cardiovascular diseases. Concept of prostaglandins.

4.3.**Dicarboxylic saturated acids** - chemical properties. Representatives: oxalic acid, malonic acid, succinic acid, glutaric acid and adipic acid). Unsaturated dicarboxylic acids - fumaric and maleic acids. Aromatic dicarboxylic acids: phthalic acid, isophthalic acid and terephthalic acid.

4.4.**Hydroxycarboxylic (fatty and aromatic) acids** – structure and properties. Stereoisomerism of fatty hydroxycarboxylic acids. Representatives: lactic acid, β–hydroxybutyric acid, tartaric acid and citric acid. Optical activity. Enantiomers and racemates. Fischer's projection formulae. Relative configuration to glycerolaldehyde. Molecules with more than one chiral centers Diastereomers. Derivatives of salicylic acid as medicines - methyl salicylate, aspirin, salol, paraaminosalicylic acid.

4.5.**Aldehyde and ketocarboxylic acids -** structure and properties. Representatives: glyoxalic acid, pyruvic acid, acetoacetic acid (tautomerism) and oxaloacetic acid. Acetoacetic ester (tautomerism). Acids involved in Kreb's cycle. Ketone bodies.

4.6.**Derivatives of carbonic acid:** carbamic acid, urethanes, carbamide (urea), urethanes, ureides, biuret, guanidine, creatine, creatinine - structure and biological meaning.

4.7.**Lipids.** Saponifiable lipids - classification. **Fats** - structure and properties. β–Oxi-dation. Saponification of triglycerides. Types of phospholipids. Glycerophospho-lipids: cephalins and lecithins. Biological meaning.

5. Amines

5.1.Aliphatic and aromatic amines. Structure and basicity of amines. Physical and chemical properties of amines. Biogenic amines. Amides, Schiff's bases, diazonium salts, and azo-compounds (azo-dyes). Amides with medical usage: phenacetin and paracetamol.

5.2.**Aminoalkohols:** aminoethanol (colamine), choline and sphingosine. Acetyl-choline. Catecholamines: dopamine, noradrenalin, adrenaline.

6. Amino acids and peptides

6.1. **Amino acids (I).** Classification of amino acids. Representatives. Essential amino- acids. Structure, configuration and optical activity of amino acids. Amino acids as dipolar ions. Isoelectric point. Amphoteric character of aminoacids.

6.2. **Amino acids (II).** Chemical properties: reactions of amino - and carboxylic- groups. Heat treatment of aminoacids and lactam - lactim tautomerism. Biological importantce of amino acids.

6.3. **Aromatic aminoacidsn - *p*-aminobenzoic acid.** Local anaesthetics: anaesthesin and novocain. Structural analogues of novocain – lidocain and baycain**. Sulphanilic acid and some sulphonamides:** sulphathiazole, sulphacetamide, sulphaguanidine. Concept of metabolites.

6.4. **Peptides**-structure and properties. Stereochemistry of peptide bond. Some important peptides: glutathione. Some important peptide hormones: vasopressin, oxytocin, insulin. Biological importance of peptides

7. Carbohydrates

7.1. Classification of carbohydrates. **Monosaccharides (I).** Important representatives: glucose, mannose, galactose, fructose, ribose and deoxyribose. Configuration and optical activity of monosaccharides. Anomers, epimers and mutarotation. Cyclization- hemiacetal (pyranose and furanose) formation. Haworth structures. **Vitamin C –** structure, properties and its role as antioxidant.

7.2. **Monosaccharides (II).** Chemical properties: oxidation and reduction reactions. Producing of aldonic acids, sugar acids, uronic acids and polyalcohols (sorbitol). Reactions of carbonyl and hydroxyl groups. Biologically important esters. Glycoside formation. O- and N-glycosides.

7.3. **Disaccharides.** Types of linkage of glycoside residues. Non reducing and reducing disaccharides - some important representatives (sucrose, maltose, cellobiose, lactose) - structure and properties. Galactoseaemia.

7.4. **Homopolysaccharides.** Structure and properties of starch (amylose and amylo-pectin), glycogen and cellulose. Derivatives of cellulose – cellulose nitrates and cellulose acetates.

7.5. **Heteropolysaccharides:** hyaluronic acid, chondroitinsulphuric acid and alginic acid - structure and properties. Heparin - biological meaning.

8. Hetererocyclic compounds.

8.1. Five-membered heterocycles with one heteroatom. **Pyrrole** - structure and properties. Biologically active derivatives of pyrrolidine: proline, hidroxyproline. Organic compounds containing porphin ring: protoporphirin and haem. Pyrrole pigments: haemoglobin, bilirubin.

8.2. Fused ring compounds with pyrrol ring. **Indole** – structure and properties. Important representatives with biological activity: tryptophane. Neurotransmitters and hormone derivatives of indole: tryptamine, serotonin and melatonin.

8.3. Five-membered heterocyclic compounds with two heteroatoms (diazoles) (I). **Pyrazole**-structure and properties. Derivatives of 5-pyrazolon: antipyrine, pyramidon (amidophene) and analgin. Ideas for antipyretics.

8.4. Five-membered heterocycles with two heteroatoms (diazoles) (II). **Imidazole**-structure and properties. Histidine and histamine. Antihistamine medicines. Biotin (vitamin B_7).

8.5. Six-membered heterocycles with one heteroatom. **Pyridine** (azine)-structure and properties. Pyridine carboxylic acids and their derivatives: nicotinamide (vitamin PP, vitamin B_3), coramine, tubazide, pyridoxine (vitamin B_6). Biological meaning.

8.6. Six-membered heterocycles with two heteroatoms (diazines). **Pyrimidine**-structure and properties. Barbituric acid and some barbiturates - barbital (veronal), phenobarbital (luminal), evipan. Pyrimidine bases - cytosine, uracil and thymine. Antimetabolites with antitumor activity: 5 - fluorouracil. Thiamine (vitamin B_1).

8.7. Fused ring compounds with pyrimidine ring (I). **Pteridine**-structure and derivatives: folic acid (vitamin B_9) and riboflavin (vitamin B_2).

8.8. Fused ring compounds with pyrimidine ring (II). **Purine** – structure and properties. Xanthine and hypoxanthine. Uric acid. Purine bases: adenine and guanine.

8.9. **Nucleic acids: RNA and DNA**. Hydrolysis of nucleic acids. Nucleosides and nucleotides. **Pyrimidine nucleosides:** uridine, cytidine and thymidine. **Purine nucleosides:** adenosine and guanosine. Primary and secondary structure of nucleic acids. Biological importance of nucleic acids.

8.10. **Alkaloids.** Characteristic of alkaloids. N-Methylxanthine derivatives: caffeine, theobromine, theophyline. Nicotine, atropine, cocaine, quinine and morphine. Derivatives of morphine - heroin and codeine. Physiological action.

PRACTICAL COURS IN MEDICALCHEMISTRY
FOR ENGLISH SPEAKING STUDENTS
From the Faculty of Dental Medicine
First (Winter semester)

weeks	Topics
1st	**1. CONCENTRATION OF THE SOLUTIONS** • Percent concentration (weight/weight percent, weight/ volume percent, volume/volume percent). • Molarity. Molality. • Normality. Titer. • Connection between different types of concentrations. • Dilution of solutions.
2nd	**2. AUTOPROTOLYSIS CONSTANT. ION PRODUCT CONSTANT OF WATER. pH. pH – MEASUREMENT AND CALCULATION** • Autoprotolysis constant. • Ion product of constant of water. pH- concept. pH-scale. • Calculation of pH of strong and weak acids and bases. • Colorimetric and potentiometric methods for measurement of pH.
3th	**3. BUFFER SOLUTIONS** • Quantitative characteristic of the buffer solutions. Some important buffers. • The Henderson-Hesselbalch equation. • Calculation of pH of buffer solutions. • Buffer capacity. Determination of buffer capacity. • Acidosis and alkalosis.
4th	**4. QUALITATIVE ANALYSIS OF BIOLOGICALLY ACTIVE IONS** • Analysis of biologically active cations: K^+, Ca^{2+}, Ag^+, Hg_2^{2+}, Pb^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+} and their biological role. • Analysis of biologically active anions: CO_3^{2-}, NO_2^-, $C_2O_4^{2-}$, PO_4^{3-} , urate anions and their biological role. • Analysis of dental tartar.
5th	**5. COLLOQUIUM:** • Qualitative analysis of biologically active cations and anions and their biological role; • Concentration of solutions: percent concentration, molarity, molality, normality, titer. • Autoprotolysis constant. Ion product constant of water. pH. • Calculation of pH of strong and weak acids and bases. • Buffers; The Henderson-Hesselbalch equation. • Solve of some problems associated to the concentration, pH and buffers.
	6. HYDROCARBONS

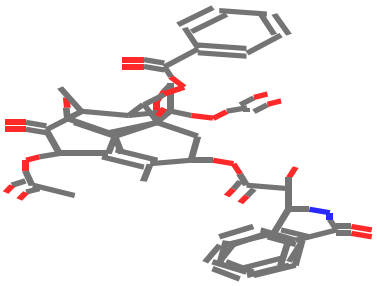
6th	• Types of organic reactions: Substitution (SR, SE, SN), addition (AN, AE), elimination (E) and rearrangement reactions. • Reaction of alkanes, alkenes, alkynes and aromatic hydrocarbons: Behavior of alkanes, alkenes and arenes towards bromine water. Electrophilic substitution reactions: brominating of benzene and toluene; nitration of benzene, toluene and naphthalene. • Oxidation of aliphatic and aromatic hydrocarbons. **Amines.** • Basicity of amines. Basicity constant. • Reactions with nitrous acid. • Diazo reaction of Ehrlich and using of this reaction in clinical practice for diagnosis. Diazonium salts. • Ring substitution in aromatic amines.
7th	**7. ALCOHOL AND PHENOLS** • Alcohols as acids and bases. Acidity of phenol. • Oxidation of alcohols and phenols. Catalytic dehydrogenation of methanol. Oxidation of hydroquinone. • Esterification of alcohols. • Demonstration of neighbour hydroxyl groups in glycerol and other polyvalent alcohols. • Electrophilic substitution of phenol (brominating and nitration). • Qualitative reaction of phenol with iron trichloride.
8th	**8. ALDEHYDES AND KETONES** • Oxidation of aldehydes and ketones. Fehling's probe, silver mirror's probe. • Reactions with phenylhydrazine and ammonia. Obtaining of phenylhydrazone. • Aldol condensation. Cannizzaro's reaction (reaction of disproportionation). • Reaction of polymerization of formaldehyde. Reaction of polycondenzation of formaldehyde with phenol and carbamide. • Legal's probe for the detection of acetone in biological materials.
9th	**. 9. CARBOXYLIC ACIDS** • Acidity of carboxylic acids. • Oxidation of carboxylic acids. Formic acid as a reducer. • Saturated and unsaturated aliphatic carboxylic acids. High fatty acids. Unsaturated Fatty acids. • Derivatives of carboxylic acids. Producing of soaps and esters. Acide amides. • Amides of the carbonic acid. • Basic properties of carbamide. Hydrolysis of urea in alkali medium. • Biuret reaction.
10th **10th**	**10. SUBSTITUTED CARBOXYLIC ACIDS** • **Hydroxycarboxylic acids: lactic acid, tartaric acid and salicylic acid.** • Ufelmann's probe for lactic acid. Diagnostic signifcance of the probe. • Reaction of potassium sodium tartarate with copper (II) hydroxide. • Reaction of salicylic acid: decarboxylation and colour reaction with $FeCl_3$ • **Keto carboxylic acids: pyruvic acid and acetoacetic acid.**

	• Colour reaction of the enol form of the acetoacetic ester. Keto-enol tautomerism of the acetoacetic ester. • Gerhard's probe for acetoacetic acid. Ketone bodies. **Amino acids.** • Structure of natural amino acids. Amino acids as dipolar ions. • Amino acids as acids and bases. Buffer action of α–amino acids. Reactions of amino acids. • Ninhydrin reaction. Biuret reaction for peptides. • Aromatic character of p-aminobenzoic acid.
11th	**11. Carbohydrates.** **I. Monosaccharides** • Monosaccharides – structure, α–inversion (epimerization). • Obtaining of osazones. • Demonstration of neighbour hydroxyl groups, oxidation of monosaccharides by Fehling's solution and by Tolens' reagent. • Detecting pentoses according Tolens. Distinction of aldoses from ketoses by the Selivanov's reaction. **II. Disaccharides and Polysaccharides**. • Disaccharides of monocarbonyl and dicarbonyl type of bonding. • Reaction of disaccharides and polysaccharides. • Inversion of sucrose. Hydrolyse of sucrose and starch.
12th	**12. Colloquium – structure and chemical properties of:** • Hydrocarbons; • Alcohols and phenols; • Aldehydes and ketones; • Carboxylic acids, substituted carboxylic acids; • Amines, amides and aminoacids.
13th	**13. HETEROCYCLIC COMPOUNDS I** • Nitrogen-containing heterocyclic compounds with five membered ring: pyrrole, indole, imidazole and pyrazole. • Colour reaction for pyrrole and indole. • Scheme of obtaining of some derivatives of 5-pyrazolon: antipyrin, pyramidone and analgin. • Colour reactions of antipyrine and pyramidon with $FeCl_3$ and HNO_2.
14th	**14. HETEROCYCLIC COMPOUNDS II** • Nitrogen-containing heterocyclic compounds with six membered ring and fused aromatic rings: pyridine, pyrimidine and purin. • Basic properties and colour reaction for pyridine. • Barbituric acid – lactam-lactim tautomerism. Qualitative reaction for detection of barbituric acid. Solubility of veronal and sedimentary reaction of veronal. • Folin's reaction for detection of uric acid and urates. • Analysis of alkaloids.
15th	**15. PRACTICAL EXAM**

Medical University- Sofia
F a c u l t y of M e d i c i n e
Department of Medical Chemistry and Biochemistry

P r o g r a m
of Medical Chemistry

for English-Speaking Students from the Faculty of Dental Medicine



I. GENERAL AND IN O R G A N I C C H E M I S T R Y

`Theoretical Bases of Medical Chemistry` - 20 hours

3. Chemical bonding and structure of molecules - 4 hours

1.1. Nature of chemical bonding. Method of valence bonds. Types of covalent bonds: σ–, π– and δ–bonds. Properties of the covalent bond. Dipole moment. Polar and no polar molecules. Delocalization of the chemical bond. Hybridization.

1.2.Nature of hydrogen bond and biological significance. Intramolecular and inter-molecular hydrogen bonds. Role of hydrogen bond for the stability and formation of biological structures. Intermolecular (ion-dipole forces, dipole-dipole forces, London dispersion forces) and ionic forces of attraction and their biological role. Metal bond.

1.3.Chemical bonds in complex compounds. Donor-acceptor (coordinative) bond. Classification and nomenclature of the complex compounds. Isomerism, structure and stability of complex compounds. Chelates in living systems. Application of certain chelates in dental practice.

1.4. Chemical bonds and electronic effects in molecules of organic compounds. Inductive and resonance (mesomeric) effects. Relationship between electronic structure and chemical properties.

4. Dispersed systems - 6 hours

2.1. Solutions and solubility. Ideal and real solutions. Solubility product constant. Units of concentration. Colligative properties of solutions: vapour pressure lowering, boiling point elevation, freezing point depression. Osmosis and osmotic pressure. Isotonic solutions.

Solutions of strong and weak electrolytes. Theory of strong electrolytes – activity and ionic strength.
2.2.Acid-base systems. Protolysis processes: Broensted-Lowry acids-bases. Conjugate acid-base pair. Acid - base strength – acid ionization constant (K_a) and base ionization constant (K_b). Lewis acids - bases.
2.3. Ionization of water. Ion product constant of water. The pH-scale. Physiological pH values. Methods for determination of pH.
2.4. Buffer solutions-properties.The Henderson-Hesselbach equation. Buffer capacity. Biological meaning of buffer solutions. Blood's buffers. Buffer solutions used in dental practice.
2.5.Hydrolysis processes. Hydrolyses of salts and organic compounds. The degree of hydrolysis and hydrolysis constant. Relationship between hydrolysis and protolysis constants. Significance of hydrolysis processes.
2.6. Colloid dispersed systems - nature, types and methods of obtaining. Dialysis. Classification of colloid dispersed systems. Solutions of high–molecular compounds. Structure of the hydrophobic colloid particles. Kinetic, optical and electric properties. Electrophoresis. Stability and coagulation of colloid solutions. Biological meaning. Reversible and irreversible hydrocolloids (alginates) used as elastic impression materials in dentistry.

3. Chemical kinetics and chemical equilibrium - 4 hours

3.1. Chemical reaction rate. Dependence of reaction rate on concentration of reactants. Rate law. Rate constant. Reaction mechanisms and rate-determine step. Reaction order. Rate equations of different reaction order. Effect of temperature on the rate of chemical reactions. A reaction energy diagram. Transition state. Activation energy- Arrhenius equation.
3.2. Catalysis. Theory of catalytic processes in point of view of transitional state. Mechanism of homogeneous and heterogeneous catalysis. Role of the catalysts in vital processes - biocatalysis.
3.3. Criteria for determination of direction of chemical processes and principles thermodynamics quantities: enthalpy, entropy and free energy. Spontaneity of chemical reactions and free energy. Exergonic, endergonic and anergonic processes. Conjugated processes. Compounds with macroergic bonds. Anergonic processes in living organisms. Chemical equilibrium. The concept of equilibrium: the forward and the reverse reaction. The equilibrium constant and change in free energy (reaction isotherm of van't Hoff). Factors affecting equilibrium. Le Châtelier's principle and chemical equilibrium.

4. Processes of electron transfer - 4 hours

4.1. Valency and oxidation number. Reactions of oxidation and reduction. Electron exchange and types of redox processes. Galvanic cell of Daniell. Galvanic cell in the oral cavity. Electrode potential. Electromotive force of galvanic element. Nernst's equation. Direction of redox processes. Relationship between redox-potential and equilibrium constant. Redox systems in living organisms. Characteristics of biological oxidation.
4.3. Corrosion. Types of corrosion. Biochemical corrosion. Nature of the electrochemical corrosion. Oral electrogalvanic element in cases of bimetallism and polymetallism. Methods for prevention of corrosion.

5. Surface phenomena - 2 hours

Adsorption. Surface energy and surface tension. Adsorption on the surface: liquid/gas; liquid/liquid; liquid/solid substance. Adsorption equilibrium. Adsorption isotherm. The Langmuir equation. Ionexchange and selective adsorption. Lyotropic series. Surface-active substances and their use in dentistry. Types of chromatography and application.

II. O R G A N I C C H E M I S T R Y - 25 hours

1.Hydrocarbons - 4 hours

1 . 1. **Saturated hydrocarbons.**

Alkanes - structure. Conformational isomerism. The reactivity of alkanes. Mechanism of reactions of free radical substitution (S_R) (halogenation of alkanes). Free radicals and carcinogenesis. Cycloalkanes: cyclohexane - conformation.

1.2. **Unsaturated hydrocarbons.**

Alkenes and alkynes: structure and properties. Stereoisomerism: geometrical (*cis - trans*) isomerism. Acidity of alkynes. Mechanism of electrophilic addition to double bond (A_E). Oxidation, reduction and polymerization of alkenes and alkynes. Mechanism of polymerization. Plastics as the most used dental materials.

1.3. **Aromatic hydrocarbons.**

Structure of benzene. Hueckel's rule of aromaticity. Mechanism of electrophilic aromatic substitution (S_E). Activators and deactivators. Orientation in benzene ring. Fused aromatic hydrocarbons. Carcinogens.

2. Alcohols, phenols and thiols -2 hours

Structures and reactivity of alcohols and phenols. Alcohols as acids and bases. Acidity of phenols. Mechanism of esterification. Bio-oxidation of methanol, ethanol and glycol. Mercaptans (thioalcohols), thioethers: physical and chemical properties. Oxidation. Mercaptans (thioplastic materials) used as impression materials in dentistry.

3. Carbonyl compounds -2 hours

Aldehydes and ketones. Reactivity and comparative review of chemical properties of aldehydes and ketones: nucleophilic addition (A_N), oxidation and reduction. Important aldehydes and ketones. Reactions of polymerization and polycondenzation. Aldol condensation and its role in the biological processes. Cannizzaro's reaction. Use of some carbonyl compounds in dental practice. Quinones-structure and properties. Phylloquinone (vitamin K_1).

Carboxylic acids - 4 hours

4.1. **Saturated monocarboxylic fatty acids and aromatic monocarboxylic acids.** Important representatives: formic acid, acetic acid, propionic acid, butyric acid, valeric acid (pentanoic acid) and benzoic acid. Chemical properties. Relationship between structure and acidity.

4.2.**Unsaturated monocarboxylic fatty acids:** chemical properties and representatives: acrylic acid, methacrylic acid and oleic acid. Polyunsaturated essential fatty acids: linoleic, linolenic, arachidonic, eicozapentaenoic and docozahexaenoic acids (Vitamin F). Role of polyunsaturated ω-3 fatty acids for prevention of cardiovascular diseases. Concept of prostaglandins.

4.3. **Dicarboxylic saturated acids.** Chemical properties. Representatives: oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid. Unsaturated dicarboxylic acids - fumaric and maleic acids. Aromatic dicarboxylic acids.

4.4. **Substituted carboxylic acids.** Hydroxycarboxylic (fatty and aromatic) acids -structure and properties. Representatives: lactic acid, β–hydroxybutyric acid, tartaric acid and citric acid. Optical activity. Enantiomers and racemates. Fischer's projection formulae. Relative configuration to glycerolaldehyde. Molecules with more than one chiral centers Diastereomers. Derivatives of salicylic acid as medicines- methyl salicylate, aspirin, salol, paraaminosalicylic acid. Aldehyde and ketocarboxylic acids - structure and properties. Representatives: glyoxalic acid, pyruvic acid, acetoacetic acid. Acetoacetic ester (tautomerism). Acids involved in Kreb's cycle. Ketone bodies.

4.5. **Derivatives of carbonic acid:** carbamic acid, carbamide (urea), urethanes, ureides, burette, guanidine, creatine, creatinephosphate, creatinine- structure and biological meaning.
4.6. **Derivatives of carboxylic acids: salts (soaps), esters, amides.** Types of esters: waxes and fats. **Fats-** structure and properties. β– Oxidation. Saponification of triglycerides. Types of phospholipids. Glycerophospholipids: cephalins and lecithins. Biological significance.

5. Amines, amides and aminoalcoholes - 2 hours

5.1.**Aliphatic and aromatic amines.** Structure and basicity of amines. Physical and chemical properties of amines. Biogenic amines. Amides, Schiff's bases, diazonium salts, and azo-compounds (azo-dyes). Amides with medical usage: phenacetin and paracetamol. **Aminoalkohols:** aminoethanol (colamine), choline and sphingosine. Acetylcholine. Catecholamine: dopamine, noradrenalin, adrenalin.
5.2.**Sulphanilic acid and sulphonamides.** Concept of metabolites.
Some representatives: sulphathiazole, sulphacetamide, sulphaguanidine.

6. Amino acids and peptides - 2 hours

6.1. Amino acids. Classification of amino acids. Representatives. Essential amino acids. Structure, configuration and optical activity of amino acids. Amino acids as dipolar ions. Amphitricha character, pKa and pI constants. Chemical properties-reactions of amino- and carboxyl- groups. Heat treatment of aminoacids and lactam-lactim tautomerism. Biological importance of amino acids.
Aromatic aminoacids - *p*-aminobenzoic acid. Local anaesthetics : anesthesin and novocain. Structural analogues of Novocain - lidocain and baycain and their use in dental practice.
6.2. Peptides-structure and properties. Stereochemistry of peptide bond. Some important peptides: glutathione. Some important peptide hormones: vasopressin, oxytocin, insulin. Biological significance of peptides

7. Carbohydrates - 4 hours

7.1. Classification of carbohydrates. **Monosaccharides.** Configuration and optical activity of monosaccharides. Anomers, epimers and mutarotation. Cyclization- hemiacetal (pyranose and furanose) formation. Haworth structures. Representatives: glucose, fructose, mannose, galactose, ribose and desoxyribose. Chemical properties of monosaccharides: oxidation and reduction. Reactions of carbonyl and hydroxyl groups. Biologically important esters. Glycoside formation. O- and N-glycosides. Vitamin C – structure, properties and its role as antioxidant.
7.2. **Disaccharides.** Types of linkage of glycoside residues. No reducing and reducing disaccharides - some important representatives (sucrose, maltose, cellobiose, lactose) - structure and properties. Galactoseaemia.
7.3. **Homopolysaccharides.** Structure and properties of starch (amylose and amylo-pectin), glycogen and cellulose. Derivatives of cellulose – cellulose nitrates and cellulose acetates. **Heteropolysaccharides:** hyaluronic acid, chondroitinsulphuric acid and alginic acid-structure and properties. Heparin - biological meaning.

8. Heterecyclic compounds - 5 hours

8.1. Five-membered heterocycles with one heteroatom. **Pyrrole -** structure and properties. Biologically active derivatives of pyrrolidine: proline, hidroxyproline, pyramem. Organic compounds containing porphin ring: protoporphirin and haem. Pyrrole pigments: haemoglobin, bilirubin. Fused ring compounds with pyrrole ring. **Indole**-structure and properties. Important representatives with biological activity: tryptophane. Neurotransmitters and hormone derivatives of indole: tryptamine, serotonin and melatonin.
8.2. Five-membered heterocyclic with two heteroatoms (diazoles) (I). **Pyrazole-** structure and properties. Derivatives of 5-pyrazolon: antipyrine, pyramidon (amidophene) and analgine. Ideas for antipyretics.

8.3. Five-member heterocycles with two heteroatoms (diazoles) (II). **Imidazole-**structure and properties. Histidine and histamine. Antihistamine medicines. Biotin (vitamin B_7).
8.4.Six-membered heterocycles with one heteroatom (azine). **Pyridine-**structure and properties. Pyridine carboxylic acids and their derivatives: nicotinamide (vitamin PP, vitamin B_3), coramine, tubazide, pyridoxine (vitamin B_6). Pyrimidine salts - used as disinfection means in dental practice.
8.5.Six-membered heterocycles with two heteroatoms (diazines). **Pyrimidine**-structure and properties. Pyrimidine bases - cytosine, thymine and uracil. Barbituric acid and barbiturates. Antimetabolites with antitumor activity: 5- fluorouracil. thiamine (vitamin B_1).
8.6.Fused ring compounds with pyrimidine ring. **Pteridine -** structure and derivatives: folic acid (vitamin B_9) and riboflavin (vitamin B_2). **Purine**– structure and properties. Xantine and hypoxanthine. N-methylxanthine derivatives: caffeine, theobromine, theophyline. Uric acid. Purine bases: adenine and guanine.
8.7. **Nucleic acids: RNA and DNA.** Hydrolyses of nucleic acids. Nucleosides and nucleotides. Pyrimidine nucleosides: uridine, cytidine and thymidine. Purine nucleosides: adenosine and guanosine. Primary and secondary structure of nucleic acids. Biological importance of nucleic acids.
8.8. **Alkaloids.** Characteristic of alkaloids. Nicotine, atropine, cocaine, quinine and morphine. Derivatives of morphine - heroin and codeine. Physiological effect.

Literature:

1. Medical chemistry. Theoretical course for students. M. Nikolov, Iv. Ivanov, M.Matova, R.Tomova, Ts.Tsanova. Medical University, Sofia“, Publishing House, Pedagog 6”, Sofia, 2011.
2. Practical Course of Chemistry for English speaking students. The authors are from the Department of Medical Chemistry & Biochemistry, Faculty of Medicine, Medical University, Sofia, Published by “Reko”, Sofia 2009.