***Syllabus for the State Exam***

1. **PHARMACOGNOSY**

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| **№** | **Topic** |
|  | Nature, object, objectives and tasks of Pharmacognosy. Systems in the Pharmacognosy. Basic concepts and approaches. |
|  | Pharmacognosy as a multidisciplinary science. Development of Pharmacognosy in Republic of Bulgaria. |
|  | Medicinal plants and herbal substances. Basic concepts and classification. Nomenclature. |
|  | Contemporary approaches to discover new medicinal plants - screening programs, ethnopharmacology and ethnobotany, ethnomedicine. Chemotaxonomic and phylogenetic approaches. |
|  | Products of natural origin. Basic concepts and classification: herbal substances, herbal preparations, herbal teas, essential oils, fats, extracts. |
|  | Products of natural origin. Obtaining identification, quality tests. Basic legal provisions in the Republic of Bulgaria. |
|  | Medicinal plants as raw plant material. Rules and requirements for collection, primary processing, packaging and storage of plant materials. |
|  | Wild plants as a source for the herbal preparations and herbal substances - biodiversity and characterization. |
|  | Cultivation of medicinal plants: introduction and acclimatization. Plant tissue culture. Cultivation of medicinal plants under controlled conditions. |
|  | European Pharmacopoeia. The purpose, tasks and structure of the European Pharmacopoeia. Herbal substances, herbal preparations, herbal medicinal products, traditional herbal medicinal products. |
|  | Morphological and anatomical diagnostic features for the characterization of the different types of herbal substances. |
|  | Macroscopic methods of analysis. Morphological and anatomical diagnostic features for the characterization of the different types of herbal substances. |
|  | Microscopic methods of analysis. Morphological and anatomical diagnostic features for the characterization of the different types of herbal substances. |
|  | Pharmacognostic analysis of herbal substances. Indicators and methods: loss on drying; determination of total ash content, ash content insoluble in hydrochloric acid, swelling index, bitterness, microbial contamination. |
|  | Herbal medicinal products. Definition and classification. Types of herbal medicines: definition, sources and methods of production, recognition and analysis. |
|  | Place of the herbal medicinal products and herbal preparations in Ph. Eur. Basic legal provisions in R Bulgaria: Law on Medicinal Products in Human Medicine |
|  | Quality, efficacy and safety of herbal medicinal products. Purpose and objectives, requirements and quality control. |
|  | Determination of biologically active compounds in herbal substances and herbal preparations. Purpose and objectives of the qualitative and quantitative analysis. |
|  | General methods for the isolation of biologically active compounds. |
|  | Contemporary approaches for study the chemical structure of the new compounds of plant origin. |
|  | Biologically active compounds of natural origin. Chemical composition of the plants. Primary metabolites. |
|  | Biologically active compounds of natural origin. Chemical composition of the plants. Secondary metabolites. |
|  | Biologically active compounds of natural origin. Basic biosynthetic pathways. |
|  | Accumulation of biologically active compounds in plants - dynamics and factors influencing accumulation. Localization in the whole plant, parts and tissues. |
|  | Carbohydrates. General characteristics and classification. Herbal substances and herbal medicinal products containing monosaccharides. Action and application. |
|  | Carbohydrates. Oligosaccharides. Plant fibers. Plant gums and mucilage. Herbal substances containing carbohydrates. Herbal medicinal products and herbal preparations. Action and application. |
|  | Carbohydrates. Homopolysaccharides and heteropolysaccharide. Herbal substances containing carbohydrates. Herbal medicinal products and herbal preparations. Action and application. |
|  | Lipids. Glycerides, fat-substances - waxes and phospholipids. Herbal substances containing lipids. Herbal medicinal products and herbal preparations. Action and application. |
|  | Vegetable fatty oils (Olea herbaria) – not drying, semi-drying and drying. Oils with specific action. |
|  | Phenols. Herbal substances and herbal medicinal products containing phenols. Action and application. |
|  | Flavonoids. Classification. Flavonoids, isoflavonoids and neoflavonoids. Biogenesis. Isolation, identification and analysis. Relationship between chemical structure and therapeutically action. |
|  | Flavonoids. Herbal substances containing flavones, flavonols, flavonol glycosides, flavanones, dihydroflavonols, chalcones, proanthocyanidins and cyanidines. Action and application. |
|  | Flavonoids. Herbal medicinal products and herbal preparations. Action and application. |
|  | Coumarins and furanocoumarins. Herbal substances and herbal medicinal products containing coumarins and furanocoumarins. Action and application. |
|  | Tannins. Herbal substances and herbal medicinal products containing hydrolysable tannins. Action and application. |
|  | Tannins. Herbal substances and herbal medicinal products containing condensed tannins. Action and application. |
|  | Terpenes. Herbal substances and herbal medicinal products containing mono-, sesqui-, di-, tri- and tetraterpenes. Action and application. |
|  | Terpenes. Herbal substances and herbal medicinal products containing iridoids and sesquiterpene lactones. Action and application. |
|  | Essential oils. Herbal preparations. Action and application. |
|  | Essential oils. Herbal substances and herbal medicinal products containing essential oils. Action and application. |
|  | Resins and balsams. Herbal substances and herbal medicinal products containing resins and balsams. Action and application. |
|  | Quinones. Herbal substances and herbal medicinal products containing quinones. Action and application. |
|  | Anthraquinones. Herbal substances and herbal medicinal products containing anthraquinones. Action and application. |
|  | Sterols. Herbal substances and herbal medicinal products containing sterols. Action and application. |
|  | Cardiac glycosides. Herbal substances and herbal medicinal products containing cardenolides. Action and application. |
|  | Cardiac glycosides. Herbal substances and herbal medicinal products containing bufadienolides. Action and application. |
|  | Saponins. Herbal substances and herbal medicinal products containing steroid saponins. Action and application. |
|  | Saponins. Herbal substances and herbal medicinal products containing triterpene saponins. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing alkaloids with a nitrogen atom in the side chain. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing tropane alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing quinolizidine and quinoline alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing isoquinoline alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing indole alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing purine alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing imidazole alkaloids. Action and application. |
|  | Alkaloids. Herbal substances and herbal medicinal products containing steroidal alkaloids. Action and application. |
|  | Alkaloids. Plant substances containing pyrrolizidine alkaloids. Action and application. |
|  | Vitamins. Plant substances containing vitamins. Action and application. |

1. **PHARMACOLOGY**

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| **№** | **Topic** |

**GENERAL PHARMACOLOGY**

1. Types of drug transport in the body. Drug absorption and drug distribution - factors affecting drug absorption and distribution. Understanding for Physiologically-Based Pharmacokinetic (PBPK) Modelling.

2. Drug metabolism and factors affecting drug metabolism. Mechanisms of drug excretion and factors affecting drug excretion.

3. Drug dosage regimens. Pharmacokinetic modelling. Model-independent and basic pharmacokinetic parameters, their assessment and value for pharmacotherapy. Multiple drug administration. Population pharmacokinetic modelling and therapeutic drug monitoring.

4. Mechanisms for realization of drug activity. Quantitative (graded) and quantal (population) dose (concentration) – response relationship. Therapeutic index.

5. Drug interactions.

6. Adverse drug reactions. Classification. Drug safety and Pharmacovigilance.

7. Phases in drug development. Non-clinical tests of new drugs. Clinical trials of drugs.

8. Pharmacogenomics, pharmacogenetics and gene therapy.

**SPECIAL (SYSTEMS) PHARMACOLOGY**

9. Muscarinic agonists (М-cholinomimetics, parasympaticomimtics). Inhibitors of acetylcholinesterase. Muscarinic antagonists (М-cholinolytics, parasympatholytics).

10. Neuromuscular blockers and centrally acting miorelaxants. General and local anaestethics. Safety profile.

11. Alpha-adrenomimetics (sympathomimetics). Alpha-adrenolytics (sympatholytics). Beta-adrenomimetics. Beta-adrenolytics. Pharmacogenetic aspects.

12. Аntihistamines and antimigraine drugs. Endothelin-1 antagonists.

13. Sedative-hypnotic and anxiolytic drugs. Safety profile.

14. Antidepressant drugs, antipsychotic drugs and mood-stabilizing drugs. Safety profile.

15. Antiepileptic drugs. Drugs for Neurodegenerative diseases (Parkinson’s disease, Huntington’s disease and Alzheimer’s disease). Safety profile.

16. Opioid analgetics. Nonsteroidal antiinflammatory drug agents’ (NSAID) and non-opioid analgesics and antipyretics. Safety profile.

17. Antirheumatic agents. DMAD and anticytokine agents. Drugs for gout. Antiosteoporotic drugs. Safety profile.

18. Immunomodulators and immunosuppressants. Glucocorticosteroids and mineralcorticoids. Safety profile.

19. Drugs for treatment of heart failure. Recombinant human B-natriuretic peptide. Antianginal drugs for ishemic heart disease. Pacemaker inhibitors. Safety profile.

20. Lipid-lowering drugs. Antihypertensive drugs. Diuretics. Safety profile.

21. Calcium channel blockers and vasodilators. Antiarrhythmic drugs. Angiotensin-converting enzyme inhibitors. Angiotensin AT1 – receptor blockers. Direct renin inhibitors. Safety profile.

22. Hematopoietic drugs. Anticoagulant, antiplatelet and fibrinolytic drugs. Anti-anaemic drugs with iron, folic acid and vitamin В12. Hematopoietic growth factors. Safety profile.

23. Drugs for Respiratory Tract disorders – Asthma, COPD. Antitussives and expectorants.

24. Drugs for Gastrointestinal Tract Disorders. Drugs for treatment of peptic ulcer disease. Antiemetic agents. Prokinetic drugs, drugs for treatment of constipation and antidiarrheal agents. Safety profile.

25. Drugs for treatment of hypo- and hyper-thyroidism. Safety profile.

26. Insulin drug products. Oral antidiabetic agents. Incretin mimetics and synthetic analogs of amylin. Drugs for treatment of obeistas. Safety profile.

27. Female sex hormones, therapeutic applications. Hormonal contraception. Hormonal replacement therapy (HRT). Uteroactive drugs. Male sex hormones, therapeutic applications. Anabolic steroids. Overview of treatment of erectile dysfunction. Safety profile.

28. Aminoglycosides. Sulfonamides. Trimethoprim. Tetracyclines and glycylcyclines. Chlorampenicol. Streptogramins and oxazolidinones. Safety profile.

29. Beta-lactam antibiotics. Cephalosporines and other beta-lactams. Bacitracin. Vancomycin and Safety profile.

30. Macrolides, ketolides and macrocyclic macrolides. Lincosamides. Fusidic acid. Pleuromutilins. Safety profile.

31. Fluoroquinolones. Metronidazole. Nitrofurantion. Polymixins and lipoglycopeptides. Safety profile.

32. Antituberculosis agents. Antileprosy drugs. Safety profile.

33. Antiviral drugs. Safety profile.

34. Antimycotic drugs. Safety profile.

35. Antiprotozoal agents: for treatment of trichomoniasis, toxoplasmosis and amebiasis. Antimalaria and antihelmintic drugs. Safety profile.

1. **TOXICOLOGY**

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| **№** | **Topic** |
| 1. | Basic concepts in toxicology. Toxic substances. Intoxication. Toxic effects and interactions. |
| 2. | Toxicometry. Quantitative characteristics of the toxic action. |
| 3. | Intake of toxic substances. Factors influencing intake of toxic substances. Absorption and distribution - physico-chemical mechanisms. Blood-brain barrier. |
| 4. | Metabolism of xenobiotics. General characteristics of metabolic processes. Types of reactions from Phase 1 and Phase 2. Factors affecting drug metabolism. |
| 5. | Metabolism of xenobiotics - Phase 1 reactions. Enzyme systems. Significance for drug metabolism and drug toxicity. |
| 6. | Metabolism of xenobiotics - Phase 2 reactions. Enzyme systems. Significance for drug metabolism and drug toxicity. |
| 7. | Elimination of toxic substances and metabolic products. Routes of elimination and peculiarities. Extracorporeal methods for cleansing the body of toxic substances - hemodialysis, plasmafiltration, carbohemoperfusion. Use in the treatment of acute drug intoxications. |
| 8. | Toxicodynamics. Mechanisms of toxic action. Toxic effect on enzyme systems, interaction with biological macromolecules. |
| 9. | Carcinogenesis. Teratogenesis. Immunotoxicity, gene toxicity. |
| 10. | Haematoxic substances. Representatives. Mechanism of toxic action. Antidotes. |
| 11. | Hepatotoxic substances. Toxic damage to liver function. |
| 12. | Toxic action of paracetamol. Mechanism. Antidote therapy. |
| 13. | Intoxication with medicines, acting on the CNS. Benzodiazepines. |
| 14. | Toxic effect of ethanol. |
| 15. | Intoxication with methanol and ethylene glycol. Mechanism. Antidote therapy. |
| 16. | Toxic action of organophosphorus compounds and carbamates. Mechanism. Antidote therapy. |
| 17. | Toxic action of metals. Acute and chronic poisoning. |
| 18. | Toxic action of amphetamines and cocaine. |
| 19. | Toxic action of opiates. Acute poisoning, abstinence and substitution therapy. |
| 20. | Poisoning with toxins of plant, animal and bacterial origin. Mushroom intoxications. Snake poisons. Botulism. |

***Bibliography***

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***Main sources:***

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2. J. Bruneton. Pharmacognosy, Phytochemistry, Medicinal Plants. Intercept Ltd., 1999.

***Additional sources:***

1. ЕМА - List of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products
2. EMA. Council of Europe. European Pharmacopoeia: 11th ed. Strasbourg: Council of Europe; 2022.
3. EMA. HMPC monographs: Overview of recommendations for the uses of herbal medicinal products in the paediatric population. EMA/HMPC/228356/2012 (July 2018)
4. Reichling, J. (eds.). 2003. Hagers Handbuch der Drogen und Arzneistoffe.,Hager ROM 2003; 195-9.
5. WHO 2007. Monographs on selected medicinal plants , Vol. 3, Geneva, 390.
6. WHO 2009. Monographs on selected medicinal plants ,Vol. 4, Geneva, 448.
7. WHO. 1999. Monographs on Selected Medicinal Plants, Vol. 1. Geneva, 295.
8. WHO. 2002. Monographs on Selected Medicinal Plants,Vol. 2, Geneva.
9. WHO. 2003. Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants, Geneva, 80.
10. Wichtl, M..:2004. Herbal drug and Phytopharmceuticals (3rd English edition) Ed. MedPharm GmbH, Scientific Publishers, 195-9.
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2. Goodman & Gilman's The Pharmacological Basis Of Therapeutics. 13th ed. [John S. Lazo](http://www.allbookstores.com/author/John_S_Lazo.html) (Editor), [Louis Sanford Goodman](http://www.allbookstores.com/author/Louis_Sanford_Goodman.html) (Editor), [Alfred Goodman Gilman](http://www.allbookstores.com/author/Alfred_Goodman_Gilman.html) (Editor), [Keith L. Parker](http://www.allbookstores.com/author/Keith_L_Parker_M_d.html) (Editor). McGraw-Hill, 2018

3. Rang, HP., Dale, MM., Ritter, JM., Moore, PK. Pharmacology. 9th edition. Edinburgh: Churchill Livingstone, 2020.

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1. Timbrell, J. Principles of biochemical toxicology. Taylor & Francis, London, 2000.
2. . Casarett & Doull’s Toxicology. The basic science of poisons. (Klaassen, C. D., ed.). McGraw-Hill, New York, 2008.
3. . Barile, F.A. Clinical Toxicology – principles and mechanisms. CRC Press, Boca Raton, 2004.