

## TOXICOLOGY

MODULE	CONTENT	YEAR	TERM	CREDITS	TYPE
Medicine and Pharmacology	Toxicology	5th	1st	6	Compulsory
<b>LECTURER(S)</b>			<b>Postal address, telephone nº, e-mail address</b>		
<ol style="list-style-type: none"> <li>1. ANTONIO PLA MARTÍNEZ (CU)</li> <li>2. ANTONIO HERNANDEZ JEREZ (CU)</li> <li>3. FERNANDO GIL HERNANDEZ (CU)</li> <li>4. LOURDES RODRIGO CONDE-SALAZAR (PTU)</li> <li>5. OLGA LÓPEZ GUARNIDO (CD)</li> <li>6. PABLO OLMEDO PALMA (AD)</li> </ol>			<ul style="list-style-type: none"> <li>• Department of Legal Medicine, Toxicology and Physic Antropology Faculty of Medicine (PTS). Avenida de la Investigación, 11. 18016 - Granada. Tel: 958-243546. Fax: 958-246107 Email:</li> <li>• <a href="mailto:apla@ugr.es">apla@ugr.es</a></li> <li>• <a href="mailto:ajerez@ugr.es">ajerez@ugr.es</a></li> <li>• <a href="mailto:fgil@ugr.es">fgil@ugr.es</a></li> <li>• <a href="mailto:lourdesr@ugr.es">lourdesr@ugr.es</a></li> <li>• <a href="mailto:olga@ugr.es">olga@ugr.es</a></li> <li>• <a href="mailto:polmedopalma@ugr.es">polmedopalma@ugr.es</a></li> </ul>		
<b>DEGREE WITHIN WHICH THE SUBJECT IS TAUGHT</b>					
Degree in Pharmacy					
<b>PREREQUISITES and/or RECOMMENDATIONS (if necessary)</b>					
It is recommended to have approved the following subjects: Basic Principles of Chemistry, Inorganic Chemistry, Structural Biochemistry, Metabolic Biochemistry, Cell and Human Fisiology (I and II) and Pharmacology (I, II and III)					
<b>BRIEF ACCOUNT OF THE SUBJECT PROGRAMME (ACCORDING TO THE DEGREE ¿??)</b>					
Toxicity. Phases of toxic phenomenon. Assessment of toxicity. Analytical Toxicology. Drug toxicity.					
<b>GENERAL AND PARTICULAR ABILITIES</b>					



#### A. General skills

- Evaluate therapeutic and toxic effects of pharmacologically active substances
- Learn to apply the scientific method and acquire skills in handling legislation, sources of information, literature, development of protocols and other aspects that are considered necessary for the design and critical assessment of preclinical and clinical trials.
- Providing therapeutic counseling in dietotherapy and pharmacotherapy and in the field in nutrition and food for establishments serving.
- Identify, evaluate and assess the problems related to drugs and medications, as well as participate in pharmacovigilance activities.
- Assessing the toxicological effects of substances and to design and implement testing and tests.
- Develop communication and information skills, both oral and written, to deal with patients and users of the center where play their work. Promote job capabilities and collaboration in multidisciplinary teams and other related healthcare professionals.
- Recognize the own limitations and the need to maintain and update professional skills, with particular emphasis on self-learning of new knowledge based on scientific evidence.

#### B. Specific skills

- Use medicines safely considering its physical and chemical properties including any risks associated with their use
- Promoting rational use of medicines and health products.
- Assessing the toxicological effects of substances and to design and implement testing and tests.
- Knowing the nature, mechanism of action and effect of toxic and resources in case of poisoning.

Knowing the analytical techniques related to laboratory diagnosis, toxics, food and environment.

### **OBJECTIVES (EXPRESSED IN TERMS OF EXPECTED RESULTS OF THE TEACHING PROGRAMME)**

1. Knowledge of the fundamentals and basic principles of toxicology
2. Knowledge of the nature and mechanisms of action of the toxic effect, and the principles of treatment
3. Basic knowledge of methodology for evaluating the toxicity and the risk
4. Knowledge of analytical techniques related to the analysis of toxics
5. Knowledge of the most important aspects regarding the toxicity of drugs

### **DETAILED SUBJECT SYLLABUS**

#### **THEORETICAL SYLLABUS:**

#### **I. BASIC TOXICOLOGY**

Item 1. INTRODUCTION TO TOXICOLOGY. Concept of Toxicology. Historic milestones. Content and limits of Toxicology. Areas and Branches of Toxicology. Definitions and glossary of toxicological concepts: poisoning, toxic and toxicity. Forms of intoxication. General Etiology of poisoning. (1 h)

Item 2. THE TOXIC PHENOMENON. Phases of toxic phenomenon: exposure phase, toxicokinetics phase, toxicodynamic phase. Dose-response relationships. Chemical structure-activity relationships. Factors affecting toxicity. (1 h)



Item 3. TOXICOKINETICS (I). General: Toxicological interest of toxicokinetics. Main routes of absorption: digestive, respiratory and skin. Toxicological aspects. (1 h)

Item 4. TOXICOKINETICS (II). Distribution, binding and accumulation of toxics. Selective binding. Toxicological concern of distribution. (1 h)

Item 5. TOXICOKINETICS (III). Removing toxics: general aspects. Main routes of elimination. Elimination by the kidneys, respiratory and biliary. Other routes of elimination. Toxicological concern of elimination. (1 h)

Item 6. BIOTRANSFORMATION. Overview: metabolism as the main determinant of toxicity. Types of biotransformation reactions: Phase I and Phase II reactions. Factors affecting the biotransformation of toxics. Genetic polymorphisms and their toxicological relevance. Toxicological relevance of the phenomena of inhibition, enzyme activation and induction. (2 h)

Item 7. MECHANISM OF ACTION OF TOXICS. Overview. Selective toxicity. Classification. Main mechanisms of toxicity. (2 h)

Item 8. DIAGNOSIS AND TREATMENT OF POISONING . Biological and chemical- toxicologic diagnosis. Epidemiology of acute poisonings. General aspects of the treatment of poisoning. Local treatment. General treatment. Main methods of treatment: Principles and applications. (1 h)

## II. TOXICITY EVALUATION

Item 9. INTRODUCTION TO THE EVALUATION OF TOXICITY AND RISK. Concept. General principles for toxicity studies. General variables in the toxicological evaluation. Toxicological experimentation regulations. Classification of toxicity tests. International agencies involved. Alternative methods: Advantages and disadvantages. (2 h)

Item 10. CRITERIA OR PARAMETERS OF TOXICITY. Concept. Types: Indices of toxicity, exposure tolerable limits and maximum permissible concentrations. Determination of different parameters. Calculations. (2 h)

Item 11. RISK EVALUATION. Introduction and definitions. Methodology. Perception of risk. Risk assessment strategies. Phases of the risk assessment process. (1 h)

## III. ANALYTICAL TOXICOLOGY

Item 12. ANALYTICAL TOXICOLOGY. INTRODUCTION. Role of toxicological testing laboratory in Clinical Toxicology, Forensic Toxicology and Industrial Toxicology. Analytical implications derived from toxicokinetic aspects with special reference to the biotransformation process. (1 h)

Item 13. THE SAMPLE FOR TOXICOLOGICAL ANALYSIS. Features and applications of the different samples. Requirements for the collection and shipment of samples in Clinical, Forensic and Industrial Toxicology. (1 h)

Item 14. INTRODUCTION TO TOXICOLOGICAL ANALYSIS. Definition. Phases of toxicological analysis. Qualitative and quantitative analysis. Information. Interpretation of results. (1 h)

Item 15. EXTRACTION TECHNIQUES FOR TOXICOLOGICAL ANALYSIS (I). General. Classification of toxics



for analytical purposes. Extraction of the different types of toxic: overview. (1 h)

Item 16. EXTRACTION TECHNIQUES FOR TOXICOLOGICAL ANALYSIS (II). Methods of extraction for the different types of toxics: gaseous, volatiles, organics and inorganics. (1 h)

Item 17. TECHNIQUES USED IN THE TOXICOLOGICAL ANALYSIS (I). Introduction. Colorimetric reactions. Spectrophotometric techniques. Rationale and applications to the screening, confirmation and quantification of toxics. (1 h)

Item 18. TECHNIQUES USED IN THE TOXICOLOGICAL ANALYSIS (II). Chromatographic techniques. Rationale and applications to the screening, confirmation and quantification of toxics. (1 h)

Item 19. TECHNIQUES USED IN THE TOXICOLOGICAL ANALYSIS (III). Immunochemical techniques. Fundamentals and applications to the screening, confirmation and quantification of toxics. (1 h)

#### **IV. DRUG POISONING**

Item 20. Drug poisoning. Introduction. Etiology. Problems in diagnosis. Drugs involved in poisoning. Pharmacological / toxicological effects of drugs: therapeutic effects, side effects and toxicity. Acute toxic effects (overdose) and chronic toxicity. (1 h)

Item 21. ANALGESICS AND NONSTEROIDAL ANTIINFLAMMATORY DRUGS: SALICYLATES. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (1 h)

Item 22. ANALGESICS AND NSAIDS: PARACETAMOL AND NSAIDS. Etiology. Mechanism of action. Toxicity. Toxicological analysis (1 h)

Item 23. PSYCHOACTIVE DRUGS: ANTIDEPRESSANTS. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (2h)

Item 24. PSYCHOACTIVE DRUGS: NEUROLEPTICS. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (1h)

Item 25. PSYCHOACTIVE DRUGS: BARBITURATES. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (1h)

Item 26. PSYCHOACTIVE DRUGS: BENZODIACEPINES. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (1h)

Item 27. OTHER DRUGS. Etiology. Mechanism of action. Toxicity. Toxicological analysis. (1 h)

#### **V. OTHER TOXICS HEALTH INTEREST**

Item 28. TOXICITY OF DRUGS OF ABUSE (I). Introduction. Definitions and Concepts. Factors involved in the process of drug addiction. Ability of different drugs to produce dependency. Toxicokinetics and addictiveness. Classification. Effects of drugs of abuse: Acute Toxicity (Overdose), Effects of drugs of abuse: effects in the medium and long term. Addiction. (2 h)



Item 29. ETHYL ALCOHOL . Introduction . Physico- chemical properties. Sources of intoxication. Toxic doses . Toxicokinetics. Mechanism of action. Metabolic effects. Toxicological Research. Medico-legal aspects. (2 h)

Item 30. CARBON MONOXIDE. Introduction. Physico- chemical properties. Sources of intoxication. Etiology. Toxic doses. Pathophysiology. Symptomatology. Treatment. Toxicological Research . (1 h)

### **PRACTICAL SYLLABUS:**

#### **Seminars/ Laboratory Practice**

1. BIBLIOGRAPHIC RESOURCES IN TOXICOLOGY. Major databases in Toxicology. Using practical learning module BUSCATOX. Making assumptions. (1h)
2. DRUGS AND TRAFFIC. Effects of the main drugs on the ability to drive motor vehicles. Legislative aspects. Analytical aspects. Solving practical assumptions. (2 h)
3. INVESTIGATION OF VOLATILES. Determination of ethanol in whole blood. Chemical method. (3 h)
4. EXTRACTION OF ORGANIC TOXICS FROM BIOLOGICAL FLUIDS. Extracting a urine sample. Fractionation of the extract. (3 h)
5. IDENTIFICATION OF ILLICIT DRUGS: Cannabis and cocaine by colorimetry, UV-spectrophotometry and thin layer chromatography. (3 h)
6. DETERMINATION OF BIOMARKERS. Colorimetric determination of cholinesterase activity. (3 h)

### **READING**

#### **KEY REFERENCES:**

ELLENHORN MJ, BARCELOUX DG. Medical Toxicology, 2ª ed.. Williams & Wilkins, Baltimore, 1997.

GISBERT CALABUIG, JA. Medicina Legal y Toxicología, 6ª ed., Masson, Barcelona, 2004.

KLAASSEN CD. Casarett and Doull's Toxicology. The basic science of poisons, 7ª ed., MacGraw Hill, New York, Oxford, 2008.

KLAASSEN CD y WATKINS JB. Casarett y Doull. Fundamentos de Toxicología. McGraw Hill. Interamericana. Madrid, 2005

MARRUECOS L, NOGUÉ S Y NOLLA J. Toxicología clínica. Springer-Verlag Ibérica. Barcelona, 1993.

PLA A, HERNÁNDEZ AF, GIL F. Manual de Toxicología. Editorial Técnica Avicam. Fleming. Granada, 2016.

REPETTO M. Toxicología fundamental, 3ª ed. Díaz de Santos, Madrid, 1997.



NOGUÉ S, MUNNÉ P, NICOLÁS JM, SANZ P, AMIGÓ M. Intoxicaciones agudas. Protocolos de tratamiento. Morales y Torres editores, s.l. Barcelona, 2003.

#### **FURTHER READING:**

HAYES AW. Principles and methods of Toxicology, 5a ed., CRC Press, NewYork, 2008.

KOLLURU R, BARTELL S, PITBLADO R Y STRICOFF S. Manual de Evaluación y Administración de Riesgos. McGraw Hill, México. 1998

LAUWERYS R. Toxicología industrial e intoxicaciones profesionales. 3ª ed., Masson, 1994.

MOFFAT, OSSELTON Y WIDDOP. Clarke's Analysis of Drugs and Poisons. 3ª ed. Pharmaceutical press, London, 2004

OMS. Principles and methods for evaluating the toxicity of chemicals. Part I. Environmental Health Criteria, 6. Geneve, 1978.

REPETTO M. Toxicología avanzada. Díaz de Santos, Madrid, 1995

REPETTO G, GOTELLI C, RODRÍGUEZ VICENTE MC, DEL PESO A, GASCÓ P. Tendencias en Evaluación del Riesgo Tóxico. En: Toxicología de Postgrado. Repetto M y col. Área de Toxicología, Universidad de Sevilla, 2004.

REPETTO G y col. Evaluación toxicológica y de Riesgos específicos. En: Toxicología de Postgrado. Repetto M y col. Área de Toxicología, Universidad de Sevilla, 2004.

#### **RECOMMENDED INTERNET LINKS**

Basic Toxicology.

<http://www.ugr.es/~ajerez/proyecto>

Laboratory practice:

<http://www.ugr.es/~fgil/proyecto/index.php>

Agencia Española del Medicamento. Registro de medicamentos.

([www.agemed.es/actividad/legislacion/espana/registro.htm](http://www.agemed.es/actividad/legislacion/espana/registro.htm))

OCDE ([www.oecd.org/document](http://www.oecd.org/document))

European Chemicals Bureau (<http://ecb.jrc.it/testing-methods>)

Reglamento sobre notificación de sustancias nuevas y clasificación, envasado y etiquetado de sustancias peligrosas. OM 30/06/1998. Anexo B.

[http://www.consumo-inc.es/Seguridad/normativa/363\\_95/home.htm](http://www.consumo-inc.es/Seguridad/normativa/363_95/home.htm)

RAIS TOXICITY PROFILES. Toxicity values. RAGs. [http://rais.ornl.gov/tox/rap\\_toxp.shtml](http://rais.ornl.gov/tox/rap_toxp.shtml)

International Programme on Chemical Safety (IPCS)



<http://www.inchem.org>

Integrated Risk International System (IRIS)

<http://cfpub.epa.gov/ncea/iris/index.cfm>

Hazard Substances Database (**HSDB-TOXNET**)

<http://toxnet.nlm.nih.gov/>

International Agency for Research on Cancer (**IARC**)

<http://www.iarc.fr/>

Joint Committee FAO/OMS on food additives (JECFA). [http://www.fao.org/ag/agn/agns/jecfa\\_index\\_es.asp](http://www.fao.org/ag/agn/agns/jecfa_index_es.asp)

ATSDR (Toxicological Profiles).

[www.atsdr.cdc.gov/toxpro2.html](http://www.atsdr.cdc.gov/toxpro2.html)

