

MECHANISMS OF ACTION OF FREE RADICALS IN HEALTH AND SICKNESS	
GENERAL INFORMATION	
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Assistant/Associate	Assistant Professor Irena Jukić, MD, PhD Assistant Professor Ružica Palić Kramarić, MD, PhD Assistant Professor Saška Marcz, PhD Assistant Professor Stana Tokić, PhD Assistant Professor Marina Ferenac Kiš, PhD
Study Programme	Integrated undergraduate and graduate university study of Medicine
Status of the course	Elective
Year of study, semester	3 rd year, 5 th semester
ECTS	2
Workload (hours)	Lectures (10); Seminars (15)
Expected number of students	30
COURSE DESCRIPTION	
Course objectives	
Train students to understand the concept of free radicals, to interpret the sources and methods of their formation and the system of elimination in the human body. Familiarize students with the desirable and undesirable effects of free radicals. Enable students to independently interpret the mechanisms of action of cellular antioxidant systems and the actions of biologically active natural antioxidants.	
Enrolment requirements and entry competencies	
The student has passed the exam in Medical biology, Medical chemistry and Biochemistry 1 and attended Medical chemistry and Biochemistry 2.	
Learning outcomes at the Programme level	
1.1., 1.2., 2.1., 3.5.	
Learning outcomes (5-10)	
After attending lectures, preparing seminar paper, self-learning and successfully passing the exam, the students will be able to:	
<ol style="list-style-type: none"> 1. Interpret the basic structures and types of reactive oxygen (ROS) and nitrogen (RNS) species and their physical and chemical properties, sources of formation in cells and elimination mechanisms 2. Describe the physiological role of free radicals 3. Describe the effects of free radicals on the human body and the mechanisms of action due to environmental stress and the balance shift in cellular oxidation-reduction reactions 4. Discuss the elements of the oxidative stress assessment 5. Understand the measurement methods of free radicals and antioxidant enzymes 6. Understand the role of free radicals in the development of cardiovascular and neurological diseases, in carcinogenesis and aging 7. Distinguish between the activity of enzymatic and non-enzymatic antioxidants 	
Critically assess the role of antioxidants in prevention and treatment	
Course content	
Lectures	

Free radicals. Theory of formation of free radicals, types of free radicals. Etiological factors of the formation of free radicals. Free radicals and oxidative stress. Antioxidant defense system. Role of free radicals in health control.

Oxidative damage to biomolecules. Food energy. Cellular metabolism and damage. Role of acetyl-CoA and adenosine triphosphate (ATP) in the production of energy in the cell. Oxidative phosphorylation process. Reperfusion and free radicals. Lipid peroxidation.

Antioxidants – role in prevention and treatment. Food antioxidants. Role of vitamins in preventing the formation of free radicals. Vitamin E. Vitamin C. Beta-carotene. Antioxidant defense system (enzymes, coenzymes and cofactors). Secondary antioxidant protection.

Oxidative stress – aging and/or disease. Disorders of energy production. Xenobiotics and their role in the formation of free radicals. Xenobiotics and their role in the etiopathogenesis of aging. Enzyme inhibition. Atherosclerosis. Free radicals in the process of atherosclerosis. Free radicals and smoking. Autoxidation of biomolecules.

Free radicals in various diseases and carcinogenesis. Diabetes mellitus type 2. Inflammatory autoimmune diseases (vasculitis, inflammatory bowel disease, pancreatitis). Cardiomyopathy (alcoholic). Hypertension. Cerebrovascular insult. Parkinson's disease. Trauma. Eye diseases (age-related macular degeneration, cataract). Pulmonary diseases (cystic fibrosis, idiopathic pulmonary fibrosis). AIDS. Fanconi anemia. Malaria. Organ transplant. Malignant diseases.

Seminars

ROS and RNS - respiration, inflammation, multiple roles of nitrogen monoxide. ROS and RNS respiration. Role of nitrogen monoxide in inflammation. Low O₂ pressure. Lysosomes. Mitochondria. Carbonylation. Chlorine free radicals (ONOO⁻) Role of lysosomes and mitochondria in the formation of ROS. Hydrogen peroxide (H₂O₂).

Consequences of oxidative processes on macromolecules in cells. Xenobiotics. Mode of action of xenobiotics in the formation of free radicals. Mode of action of free radicals in cell damage. Disorders of energy production. Oxidative damage in intensive and long-term athlete training. Oxidative stress in prolonged sun exposure.

Cellular molecular sensors of oxidative stress. Cellular oxidation-reduction reactions. Balance shift in cellular oxidation-reduction reactions. Hydrogen peroxide. Superoxide. Hydroxyl OH. Peptide fragmentation.

Role of free radicals in cardiovascular and neurological diseases, ischemic reperfusion injury, diabetes and carcinogenesis. Role of free radicals in DNA damage. Role of free radicals in tumor growth. Role of free radicals in kidney disease. Damage to the arterial circulation in type 2 diabetes. Heart muscle damage. Elevated blood pressure. Neurological diseases.

Efficacy of antioxidants in controlled clinical trials. Observational studies on the application of antioxidant supplements. Physiological protective mechanism. Primary antioxidant protection. Enzymatic reactions. Superoxide dismutase. Glutathione peroxidase.

Mode of teaching

Lectures, Seminars

Student obligations

Students are expected to attend all class sessions, as well as to take all the examinations. However, they are allowed for excused absences, totalling 30% of all classes.

Monitoring student work (*alignment of learning outcomes, teaching methods, and grading*)

Teaching activity	ECTS	Learning outcome	Student activity	Assessment methods	Grade points	
					Min.	Max.

Attendance	0.3	1-8	Class attendance	Records	7.5	15
Seminar	0.2	1-8	Writing a seminar paper	Presentation	5	10
Final exam	1.5	1-8	Studying for the oral exam	Oral exam	37.5	75
Total	2				50	100

Evaluation of the final exam:

Student's answer	Grade points
The answer meets the minimum criteria	37.5
Average answer with notable mistakes	50.0
Very good answer with minor mistakes	62.5
Exceptional answer	75.0

Calculation of final grade:

Points achieved in class are combined with points achieved on the oral exam. The grading shall be carried out by using absolute distribution, i.e. shall be based on the final achievement and compared to the numerical system as follows:

A - Pass (P): 50-100 points ; B – No Pass (N): 0-49.99 points

Required reading (available in the library and through other media)

Title	Number of copies in the library	Availability through other media
1. Halliwell BB, Gutteridge J. Free radicals in biology and medicine. 4th rev. ed. Oxford University Press Country; 2007	0	
2. Rueben C. Antioksidansi [Antioxidants]. Sana; 1998	0	
3. Kulier I. Antioksidansi [Antioxidants]. (free <i>on line</i> book)	0	
4. Bradamante V, Lacković Z. Oksidativni stres i djelotvornost antioksidansa [Oxidative stress and the efficacy of antioxidants]. Zagreb: Medicinska naklada; 2002	0	

Additional reading

1. Loren K . Oral chelation, toxic metals and free radicals. (free *on line* book)
2. Dhavan V. Reactive oxygen and nitrogen species: general consideration In NK Ganguly et al (eds.) Studies on respiratory disorders, Oxidative stress in applied basic research and clinical practice. Springer Science, New York 2014:27-46
3. Harman D. Aging: a theory based on free radical and radiation chemistry. 1956
4. Hajibabaei K. Antioxidant properties of vitamin E. Ann Res Antioxid. 2016;1(2):e22
5. Ozcan A and Ogun M. Biochemistry od reactive oxygen and nitrogen species In: Basic principles and clinical significance of oxidative stress. 2015;
<http://dx.doi.org/10.5772/61193>

6. Sisein EA. Biochemistry of free radiacals and antioxidants. Sch Acad J Biosci, 2014;2(2):110-118
7. Stein G and Weiss J. Chemical effects of ionizing radiations. Nature 1948;161:650
8. Harper's Illustrated Biochemistry, 28th Ed.
9. Balta V, Kukulj M, Odeh D, Đikić D, Oršolić N. Praktikum iz fiziologije oksidacijskog stresa [Exercises in the Physiology of Oxidative Stress]. Internal script of Faculty of Science, University of Zagreb, 2017

Course evaluation procedures

Anonymous, quantitative, standardized student survey providing feedback on the course as well as on the work of course coordinators and their assistants/associates is being conducted by the QA Office of the Faculty of medicine Osijek.

Note /Other

E-learning does not count towards course contact hours, but is being used in teaching and comprises links to various web pages, as well as video and audio materials available on web pages.