

**MULTIMODAL CONTROL OF CHRONIC PAIN AND COMORBIDITIES WITH  
ATYPICAL ANALGESICS – “TWO BIRDS WITH ONE STONE”**

**Radica Stepanović-Petrović<sup>1\*</sup>, Maja Tomić<sup>1</sup>, Aleksandar Jovanović<sup>2</sup>,  
Uroš Pecikoza<sup>1</sup>, Ana Micov<sup>1</sup>, Katarina Nastić<sup>1</sup>**

<sup>1</sup>University of Belgrade – Faculty of Pharmacy, Department of Pharmacology,  
Belgrade, Serbia

<sup>2</sup>University of Nicosia – Medical School, Department of Basic and Clinical Sciences,  
Nicosia, Cyprus

<sup>3</sup>University of Nicosia – Medical School, Center for Neuroscience and Integrative  
Brain Research (CENIBRE), Nicosia, Cyprus

\*radica.stepanovic@pharmacy.bg.ac.rs

Osteoarthritis (OA) is the most common rheumatic disease, affecting over 300 million people worldwide. It causes chronic pain, disability and is commonly associated with comorbid diseases (CMD) that cause worse health outcomes, more complex management, and increased healthcare costs. Current treatments (typical/atypical analgesics) have limited efficacy and/or tolerability and usually do not affect or can even worsen CMD. In era of longer life expectancy, extended professional life and reduced pension funds in Serbia and Europe, there is a compelling need for maintaining functionality and working capability of older population. Our aim is to search for novel treatments that could concomitantly treat chronic pain and its major CMD: depression, cognitive impairment and/or cardiovascular disease (CVD). It was planned to test the effects of vortioxetine, a novel antidepressant with multimodal mechanism of action, on pain, depressive and cognitive-impairment behaviour and CV status in rat model of knee OA. Its effects will be compared to the effects of duloxetine, the only antidepressant used for pain relief in OA. Next, we will test the effects of 2-component combinations of vortioxetine/duloxetine with adjuvant treatments (regular exercise/metformin/nicotinamide), that showed the potential to alleviate pain, depression, reduced cognition and/or CVD in preclinical/clinical research. If proved effective and well tolerated, new treatment(s) could be implemented in clinical practice much faster and with significantly less investment, than those required to develop brand new drug, as they consist of drugs already approved for human use and safe, widely available and inexpensive non-pharmacologic measures.

**Acknowledgements**

This research will be conducted with support of the Science Fund of the Republic of Serbia, grant number 7751815, *Multimodal control of chronic pain and comorbidities with atypical analgesics – “two birds with one stone” - Fight\_PainAndComorb.*

## MULTIMODALNA KONTROLA HRONIČNOG BOLA I KOMORBIDITETA SA ATIPIČNIM ANALGETICIMA - „VIŠE MUVA JEDNIM UDARCEM“

**Radica Stepanović-Petrović<sup>1\*</sup>, Maja Tomić<sup>1</sup>, Aleksandar Jovanović<sup>2,3</sup>,  
Uroš Pecikoza<sup>1</sup>, Ana Micov<sup>1</sup>, Katarina Nastić<sup>1</sup>**

<sup>1</sup>Univerzitet u Beogradu – Farmaceutski fakultet, Katedra za farmakologiju, Beograd, Srbija

<sup>2</sup>University of Nicosia – Medical School, Department of Basic and Clinical Sciences, Nicosia, Cyprus

<sup>3</sup>University of Nicosia – Medical School, Center for Neuroscience and Integrative Brain Research (CENIBRE), Nicosia, Cyprus

\*radica.stepanovic@pharmacy.bg.ac.rs

Osteoarthritis (OA) je najčešća reumatska bolest, koja pogađa preko 300 miliona ljudi širom sveta. Prouzrokuje hronični bol, invaliditet i obično je povezan sa komorbiditetima koji dovode do lošijih zdravstvenih ishoda, složenijeg lečenja i povećanja troškova zdravstvene zaštite. Trenutno dostupne terapijske opcije (tipični/atipični analgetici) imaju ograničenu efikasnost i/ili lošu podnošljivost, i obično ne utiču ili čak mogu pogoršati komorbiditete. U vremenu kada su ljudski i radni vek produženi, a penzioni fondovi u Srbiji i Evropi smanjeni, postoji velika potreba za održavanjem funkcionalnosti i radne sposobnosti starije populacije. Naš cilj je da pronađemo nove terapijske opcije koje bi istovremeno mogle da leče hronični bol i njegove glavne komorbiditete: depresiju, kognitivno oštećenje i/ili kardiovaskularne bolesti (KVB). Planirano je ispitivanje efekata vortioksetina, novog antidepresiva sa multimodalnim mehanizmom delovanja, na bol, depresivno ponašanje, kognitivno oštećenje i kardiovaskularni status pacova u modelu OA kolena. Efekti vortioksetina biće poređeni sa efektima duloksetina, jedinog antidepresiva koji se koristi za ublažavanje bola kod OA. Zatim će biti ispitani efekti dvokomponentnih kombinacija vortioksetina/duloksetina sa adjuvantnim tretmanima (redovna fizička aktivnost/metformin/nikotinamid), koji su pokazali efikasnost u ublažavanju bola, depresije, narušene kognicije i/ili KVB u pretkliničkim/kliničkim istraživanjima. Ukoliko se pokaže da su efikasne i da se dobro tolerišu, nove terapijske opcije bi se mogle implementirati u kliničku praksu mnogo brže i sa znatno manje finansijskih ulaganja u poređenju sa vremenom i ulaganjima koja su potrebna za razvoj novog leka, jer se sastoje od lekova koji su već odobreni za ljudsku upotrebu i bezbednih, široko dostupnih i ekonomski povoljnih nefarmakoloških mera.

### **Zahvalnica**

Istraživanje će biti sprovedeno uz podršku Fonda za nauku Republike Srbije, projekat broj 7751815, *Multimodal control of chronic pain and comorbidities with atypical analgesics – “two birds with one stone” – Fight\_PainAndComorb.*