9TH INTERNATIONAL CONGRESS OF PATHOPHYSIOLOGY
5TH CONGRESS OF PHYSIOLOGICAL SCIENCES OF SERBIA
WITH INTERNATIONAL PARTICIPATION

PROGRAM AND ABSTRACT BOOK

9TH INTERNATIONAL CONGRESS OF PATHOPHYSIOLOGY
5TH CONGRESS OF PHYSIOLOGICAL SCIENCES OF SERBIA
WITH INTERNATIONAL PARTICIPATION

Izdavač
Fakultet medicinskih nauka
Univerziteta u Kragujevcu

Urednici
Ivan Srejović
Isidora Milosavljević

Štampa
Grafopromet doo, Kragujevac

Tiraž
200 primeraka

ISBN 978-86-7760-208-6

Kragujevac, 2023.

9TH INTERNATIONAL CONGRESS OF PATHOPHYSIOLOGY

AND

5TH CONGRESS OF PHYSIOLOGICAL SCIENCES OF SERBIA

WITH INTERNATIONAL PARTICIPATION

JULY, 4th – 6th, 2023.

BELGRADE, SERBIA

FINAL PROGRAM AND ABSTRACT BOOK

MEETING CHAIR

Jakovljevic Vladimir (Kragujevac, Serbia)

MEETING CO-CHAIRS

Andriantsitohaina Ramaroson (Montpellier, France)
Bolevich Sergey (Moscow, Russian)
Pechanova Olga (Bratislava, Slovak Republic)
Stankovic Sanja (Belgrade, Serbia)

INTERNATIONAL PROGRAM COMMITTEE

Bkaliy Ghassan (Sherbrooke, Canada)
Bosch Steffi (Nantes, France)
Brown Colin (Dunedin, New Zealand)
Bugiardini Raffaele (Bologna, Italy)
Buravkova Ludmila (Moscow, Russia)
Burgon Patrick (Doha, State of Qatar)
Buttar Harpal (Ottawa, Canada)
Dawn Buddhadeb (Las Vegas, USA)
Dhalla Naranjan (Winnipeg, Canada)
Falcon Juan Manuel (Derio, Spain)
Guven Celal (Adiyaman, Turkey)
Kirshenbaum Lorrie (Winnipeg, Canada)
Kreft Marko (Ljubljana, Slovenia)
Kukreja Rakesh (Richmond, USA)
Lionetti Vincenzo (Pisa, Italy)
Muntean Danina (Timişoara, Romania)
Peiro Concha (Madrid, Spain)
Pierce Grant (Winnipeg, Canada)
Rabinovich Nikitin Inna (Winnipeg, Canada)
Sturza Adrian (Timişoara, Romania)
Taskin Eylem (Adiyaman, Turkey)
Teixeira Jose (Coimbra, Portugal)
Tipparaju Srinivas (Tampa, USA)
Trifunovic Aleksandra (Cologne, Germany)
Turan Belma (Ankara, Turkey)
Tyagi Suresh (Louisville, USA)
Yilmaz Bayram (Istanbul, Turkey)

NATIONAL PROGRAM COMMITTEE

Bradic Jovana (Kragujevac, Serbia)
Djuric Dragan (Belgrade, Serbia)
Djurasevic Sinisa (Belgrade, Serbia)
Ilic Sonja (Nis, Serbia)
Joksimovic Jovic Jovana (Kragujevac, Serbia)
Medovic Rasa (Kragujevac, Serbia)
Milosavljevic Isidora (Kragujevac, Serbia)
Petrovic Anica (Kragujevac, Serbia)
Selakovic Dragica (Kragujevac, Serbia)
Sretenovic Jasmina (Kragujevac, Serbia)
Stanojevic Marija (Belgrade, Serbia)
Stojanovic Aleksandra (Kragujevac, Serbia)
Stojanovic Ljudmila (Belgrade, Serbia)
Todorovic Zoran (Belgrade, Serbia)
Trifunovic Aleksandra (Belgrade, Serbia)
Zivkovic Vladimir (Kragujevac, Serbia)

ORGANIZING COMMITTEE

Kocovic Aleksandar (Kragujevac, Serbia)
Milojevic Samanovic Andjela (Kragujevac, Serbia)
Nedeljkovic Nikola (Kragujevac, Serbia)
Nikolic Marina (Kragujevac, Serbia)
Nikolic Milos (Kragujevac, Serbia)
Ravic Marko (Kragujevac, Serbia)

FOREWORD

Dear Colleagues,

The 9th International Congress of Pathophysiology and the 5th Congress of Physiological Sciences of Serbia with international participation will be jointly held from July 4th - 6th, 2023, in Belgrade, Serbia, at Hotel Crowne Plaza. For the last 22 years, the Serbian Physiological Society has organized a series of national and internationally recognized congresses and meetings in the fields of cardiovascular biology, risk factors, and health. These meetings were recognized internationally, attracted a worldwide scientific audience, and were supported by the Federation of European Physiological Societies (FEPS), the International Union of Physiological Sciences (IUPS), and the International Society for Pathophysiology (ISP). Such success in previous years directed us to plan and organize this event in order to improve the research background and make global research cooperation easier. Our wish is to have this meeting be traditional and progressive and to attract researchers from all over the world.

This scientific meeting will cover a very diverse range of topics such as metabolic disorders, COVID-19 and post-COVID disorders, cardiovascular diseases and novel therapeutic options, immunology and inflammation, nutrition and supplementation, health care, carcinogenesis and novel therapeutic options, oxidative stress, mitochondrial function, new molecular mechanisms in pathophysiology, skin diseases, regenerative mechanisms, neurological diseases, systemic inflammatory and autoimmune diseases, and many others.

The host city, Belgrade, stands as a captivating blend of rich history, vibrant culture, and modern allure. This magnificent metropolis offers much more than meets the eye. From ancient sacral and historical sites to contemporary galleries and museums, Belgrade seamlessly merges its storied past with its dynamic present. The city's heritage dates back centuries, making it a captivating destination for both scholars and enthusiasts alike. Moreover, Belgrade's charm extends beyond its historical significance. It serves as a thriving hub for cosmopolitan living and is adorned with a tapestry of modern establishments. As the capital city of Serbia, Belgrade offers a vibrant atmosphere that caters to all tastes and interests. Belgrade has evolved into a well-developed tourist destination, attracting visitors from both near and

far. Its welcoming spirit, coupled with a wide array of accommodation options and exceptional hospitality, ensures a memorable stay for every guest. We extend our heartfelt invitation to all attendees, welcoming you to experience the warmth and allure of Belgrade and central Serbia. Immerse yourself in the captivating history, indulge in the vibrant cultural scene, and embrace the energy and beauty of this remarkable host city. We are confident that your time in Belgrade will be nothing short of extraordinary.

On behalf of the Organizing & Program Committee

Vladimir Jakovljevic
Congress President

SELECTED THIOUREA DERIVATIVES OF NAPROXEN AS POTENTIAL ANTI-INFLAMMATORY AGENTS: *IN VIVO*, *IN VITRO*, AND *IN SILICO* APPROACH

Nedeljkovic N[1], Dobricic V[2], Boskovic J[2], Vesovic M[1], Bradic J[1,3], Andjic M[1,3], Kocovic A[1,3], Jeremic N[1,3,4], Novaković J[1,3], Jakovljevic V[3,5,6], Vujic Z[2], Nikolic M[1]

[1]*Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[2]*Department of Pharmaceutical Chemistry, University of Belgrade-Faculty of Pharmacy, Belgrade, Serbia*
[3]*Center of Excellence for Redox Balance Research in Cardiovascular and Metabolic Disorders, Kragujevac, Serbia*
[4]*First Moscow State Medical, University IM Sechenov, Moscow, Russia*
[5]*Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[6]*Department of Human Pathology, First Moscow State Medical, University IM Sechenov, Moscow, Russia*

The aim of the conducted study was to develop new potential dual COX-2 and 5-LOX inhibitors based on naproxen scaffold. We performed the evaluation of *in vivo* and *in vitro* anti-inflammatory activity of newly synthesized thiourea derivatives of naproxen containing *m*-anisidine and *N*-methyl tryptophan methyl ester in a side chain. An *in vivo* study was carried out using a carrageenan-induced paw edema model of acute inflammation. COX-2 and 5-LOX inhibitory potential of synthesized compounds was evaluated using fluorometric inhibitor screening kits. *In silico* study was performed in OEDocking 3.2.0.2 software with the FRED tool. Two investigated derivatives exhibited comparable anti-inflammatory activity to naproxen (56.32%) four hours after injection of carrageenan, with the percentage of inhibition being 54.01% (*m*-anisidine derivative) and 54.12% (*N*-methyl tryptophan methyl ester derivative). *In vitro* studies of COX-2 inhibition demonstrated that none of the tested compounds achieved 50% inhibition at concentrations below 100 μM, whereas the *m*-anisidine derivative accomplished comparable inhibition of 5-LOX (IC_{50} = 0.30 μM) to commercial 5-LOX inhibitor zileuton (IC_{50} = 0.36 μM). Inability of the tested compounds to form three hydrogen bonds with ARG120 and TYR355 could be a reason why these compounds showed weak COX-2 inhibition. The *m*-anisidine derivative formed a more stable complex with the 5-LOX enzyme (−8.39 kcal/mol), compared to *N*-methyl tryptophan methyl ester derivative (−7.98 kcal/mol), with the absence of the iron ion chelation in the active site in both cases. The significant *in vivo* anti-inflammatory activity of the *m*-anisidine derivative, together with the potent inhibition of 5-LOX, highlighted this compound as a promising anti-inflammatory agent.

Keywords: naproxen, thiourea, anti-inflammatory activity, COX-2 and 5-LOX, FRED

Funding: This research was supported by the Science Fund of the Republic of Serbia, 7739840, Utilization of interplay between inflammation and cancer in the development of compounds with anticancer activity—INFCANPLAY. The research was also supported by the Ministry of Science, Technological Development and Innovation, Republic of Serbia through Grant Agreements with University of Belgrade—Faculty of Pharmacy No: 451-03-47/2023-01/200161 and with University of Kragujevac—Faculty of Medical Sciences No: 451-03-47/2023-01/200111, and by the Faculty of Medical Sciences, University of Kragujevac (Junior Project 11/20).