Anti-neuroinflammatory activity of selected 2-pyridone derivatives: *In vitro* and *in silico* study

Tanja Lunić[a], Jelena Lađarević[b], Marija Rakić[a], Vanja Veruševski[b], Biljana Božić Nedeljković[a], Dušan Mijin[b], Bojan Božić[a]

[a]Institute of Physiology and Biochemistry "Ivan Djaja", Faculty of Biology, University of Belgrade, Studentski trg 16, 11000 Belgrade, Serbia
[b]Faculty of Technology and Metallurgy, University of Belgrade, Karnegijeva 4, 11000 Belgrade, Serbia

Introduction

2-Pyridones constitute a distinctive class of heterocyclic compounds, characterized by the presence of a six-membered aromatic ring, containing a carbonyl moiety positioned in proximity to the nitrogen atom. Variously substituted 2-pyridones are **widely encountered** within both natural products and synthetic pharmaceutical agents. These compounds exhibit **notable biological activities** encompassing antimicrobial, anti-inflammatory, antioxidant, and antitumor properties. In the present study, a series of seven distinctively modified 2-pyridone derivatives were investigated *in vitro* and *in silico* with the aim of elucidating their potential in mitigating neuroinflammation and conferring neuroprotection.

Conclusion

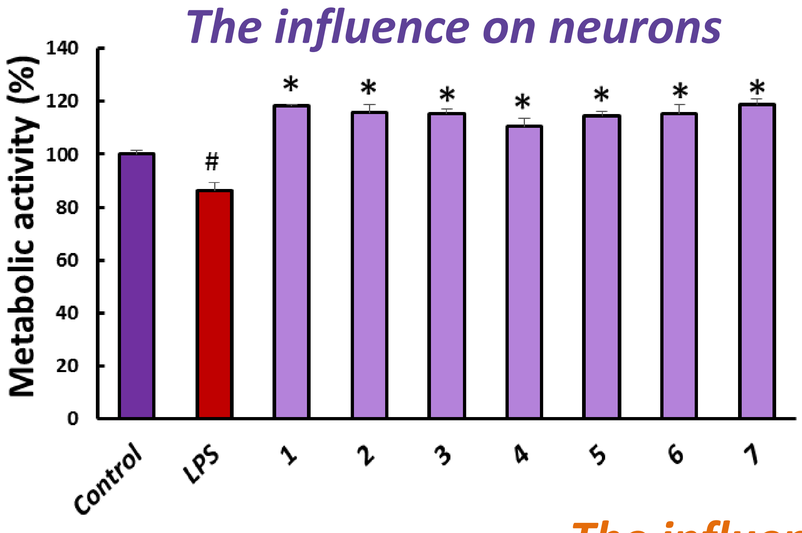
The present study indicates that investigated 2-pyridone derivatives possess the **potential to alleviate neuroinflammation** mediated by microglia and protect neighboring neurons from damage, qualifying them for further investigation in neurodegenerative diseases associated with neuroinflammation.

Methodology

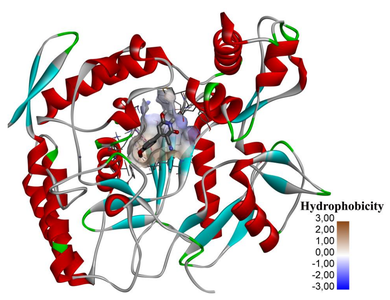
The metabolic activity of microglia and neurons was determined by MTT test, while the production of inflammatory mediators was measured by NBT, Griess, and ELISA assays. Molecular docking studies were performed in AutoDock software.

Results

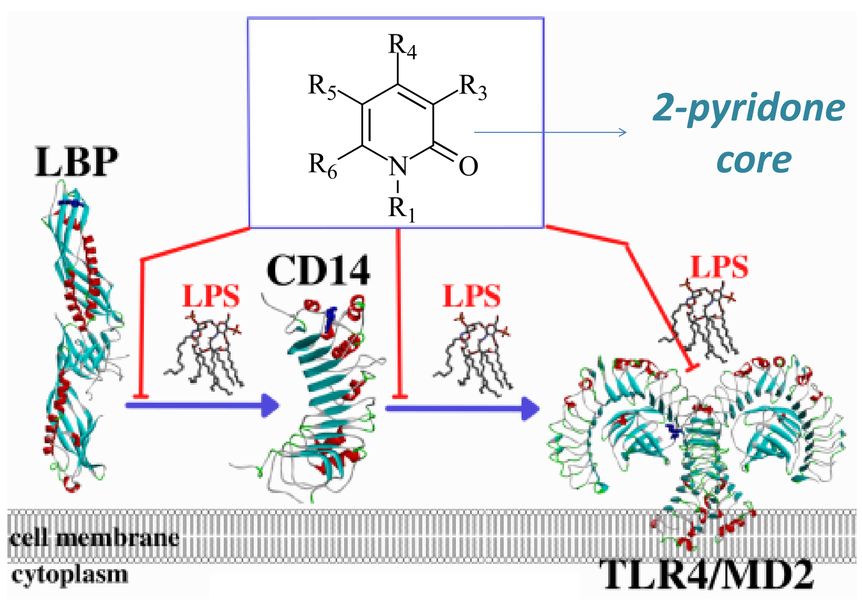
The influence on neurons



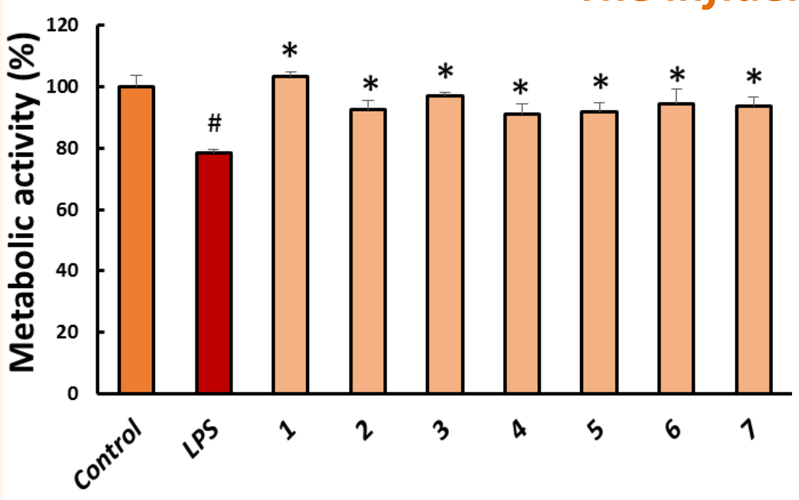
iNOS inhibition

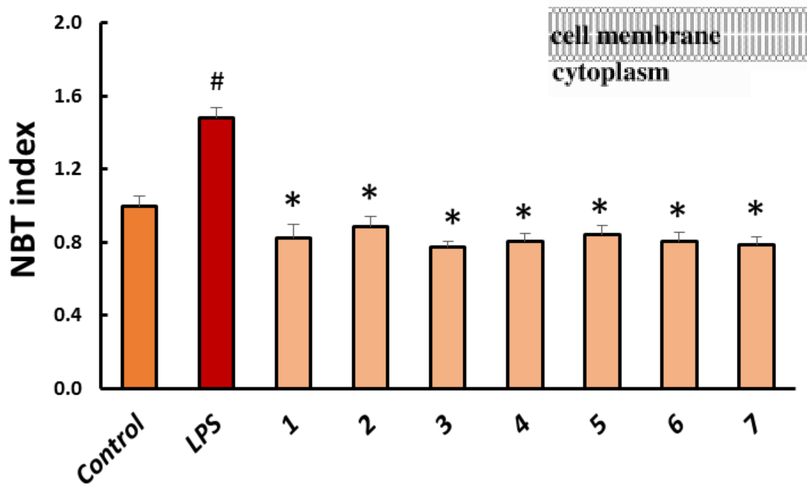


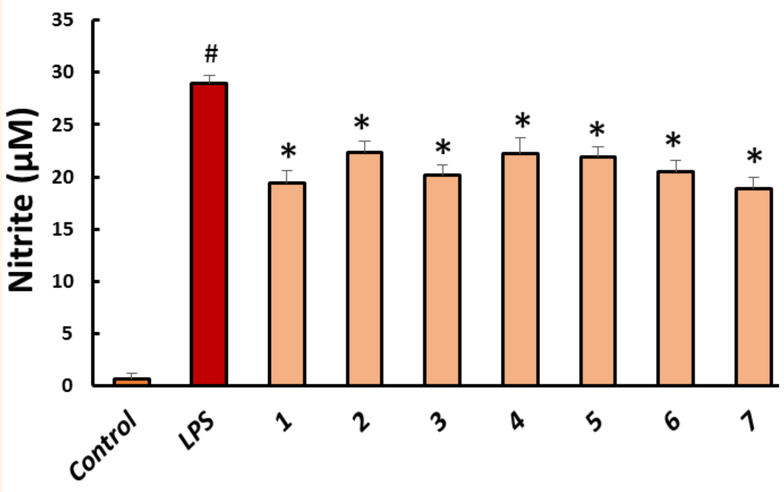
TLR4 signaling pathway inhibition

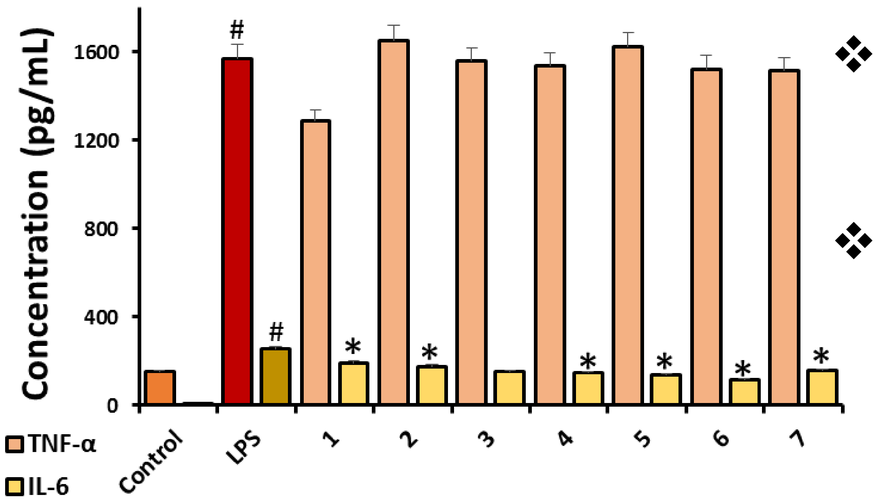


The influence on microglia









Investigated derivatives

- Increased the metabolic activity of BV2 microglia cells, as well as neurons treated with BV2 supernatants.
- Decreased the production of ROS, NO and cytokines by LPS-stimulated microglia.
- Exhibited anti-inflammatory actions through inhibition of proteins associated with the TLR4/MD2 pathway, as well as iNOS.

The 9th International Electronic Conference on Medicinal Chemistry
01–30 November 2023 | Online
MDPI