Anti-inflammatory activity of selected thiourea derivatives of naproxen on carrageenan induced paw edema in Wistar albino rats

Nikola Nedeljković [1], Vladimir Dobričić [2,*], Marina Mijajlović [1], Jovana Bradić [1], Marijana Anđić [1], Aleksandar Kočović [1], Nevena Jeremić [1], Jovana Jeremić [1], Vladimir Jakovljević [3,4], Zorica Vujić [2], Miloš Nikolić [1]

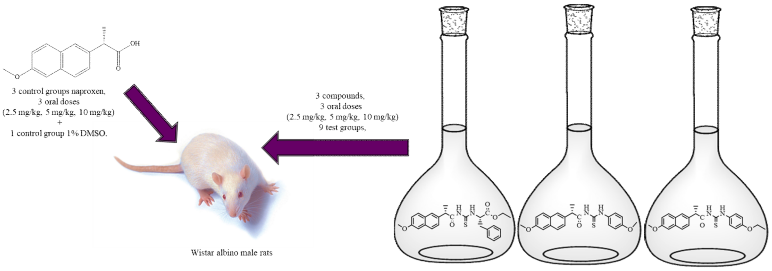
[1]*University of Kragujevac, Serbia, Faculty of Medical Sciences, Department of Pharmacy;*
[2]*Department of Pharmaceutical Chemistry, University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia;*
[3]*University of Kragujevac, Serbia, Faculty of Medical Sciences, Department of Physiology;*
[4]*Department of Human Pathology, First Moscow State Medical University IM Sechenov, Moscow, Russia;*
**Correspondence: vladimir.dobricic@pharmacy.bg.ac.rs*

INTRODUCTION

Nonsteroidal anti-inflammatory drugs are important in the treatment of many inflammatory diseases, but their therapeutic use is limited due to frequent side effects. To improve the safety profile of these drugs, new molecules with enhanced pharmacokinetic and pharmacodynamic properties are being developed in the field of medicinal chemistry. In previous studies, the thiourea derivatives of non-steroidal anti-inflammatory drugs demonstrated significant anti-inflammatory activity.

METHODS

Three thiourea derivatives of naproxen were selected from the initial group of synthesized compounds for evaluation of anti-inflammatory activity using carrageenan induced paw edema model of acute inflammation (Scheme 1). The analyzed compounds are representative molecules of our compounds set containing amino acid esters and aromatic amines in the side chain. The thickness of the left paw tissue of each rat was measured using a Digital Vernier caliper at the following time intervals: immediately before inducing inflammation and 1, 2, 3 and 4 hours after inflammation.



Scheme 1. Carrageenan induced paw edema model

RESULTS

The values of thickness of the left paw tissue in carrageenan induced paw edema model were presented as mean ± standard deviation. A statistically significant difference was defined at the level of $p < 0.05$ compared to the negative control (DMSO) (Figure 1). All tested compounds in every tested dose in the fourth hour after carrageenan administration showed a statistically significant inhibitory effect on the increase of rat paw edema compared to control, except for *L*-phenylalanine ethyl ester derivative in dose of 5 mg/kg and *p*-ethoxyaniline derivative in dose of 2.5 mg/kg. The highest percentage of inhibition was exhibited by *L*-phenylalanine ethyl ester and p-methoxyaniline derivatives (10 mg/kg) in the last hour (81.81%) (Figure 2).

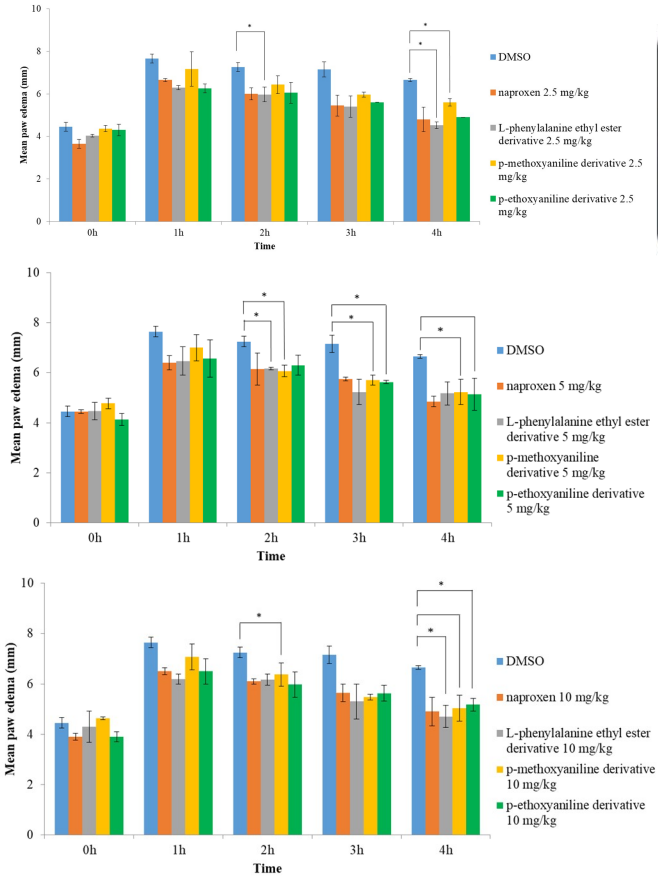


Figure 1. Effects of tested compounds on the thickness of the left paw tissue in carrageenan induced paw edema model.

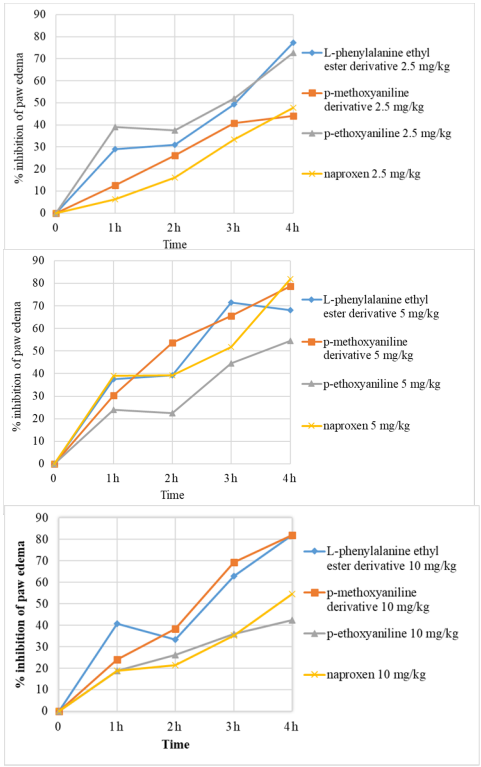


Figure 2. Percentage (%) of inhibition of paw edema by tested compounds in carrageenan induced paw edema model

CONCLUSION

According to obtained results, *L*-phenylalanine ethyl ester derivative stood out for its dose- and time-dependent anti-inflammatory effect. Upcoming research will be focused on examination of anti-inflammatory activity of the other synthesized compounds, as well as clarification of their mechanism of action.