

IN VITRO STUDIJA PROCENE ANTIOKSIDANTNE AKTIVNOSTI TETRAHIDRO-BENZO[4,5]TIENO[2,3-D]PIRIMIDINA**Jelena Lazarević^{1*}, Jelena Zvezdanović², Anelia Ts. Mavrova³,
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Oksidativni stres doprinosi razvoju i nastanku brojnih patoloških stanja, uključujući: nastanak inflamacija, ateroskleroze, dijabetesa, raka, neurodegenerativnih i kardiovaskularnih poremećaja, ali i brojnih drugih hroničnih stanja. Mnogobrojne studije potenciraju važnost upotrebe antioksidanasa i njihovu ulogu u prevenciji i lečenju bolesti koje su posledica oksidativnog oštećenja (2). Derivati tieno[2,3-d]pirimidina pokazuju čitav spektar bioloških aktivnosti: antitumorske, antiinflamatorne, antidijabetične, koje bi sve mogle biti u vezi sa antioksidativnom aktivnošću pomenutih jedinjenja. U *in vitro* studiji vršili smo procenu antioksidativnog potencijala prethodno sintetisanih i strukturno okarakterisanih jedinjenja: jedanaest tieno[2,3-d]pirimidin-4-amina (3) i šest tieno[2,3-4-d]pirimidin-4-ftalimida (4), ispitujući njihov uticaj na inhibiciju lipidne peroksidacije. Dobijeni rezultati su pokazali da među ispitanim tieno[2,3-d]pirimidinima, antioksidativna svojstva imaju samo dva jedinjenja 2-(piridin-2-il)-5,6,7,8-tetrahidrobenzo[4,5]tieno[2,3-d]pirimidin-4-amin (jedinjenje 11) i 2-(2-(piridin-2-il)-5,6,7,8-tetrahidrobenzo[4,5]tieno[2,3-d]pirimidin-4-il)izoindolin-1,3-dion (jedinjenje 17), sa vrednostima $IC_{50} = 90 \pm 4$ mM i $IC_{50} = 165 \pm 40$ mM, respektivno. Međutim, ni jedinjenja 11, niti 17 imaju antioksidativnu aktivnost uporedivu sa standardnim antioksidansima (troloks, kafeinska kiselina i kvercetin). Zajednička karakteristika jedinjenja 11 i 17, koja deluju kao inhibitori procesa lipidne peroksidacije je što su oba 2-supstituisani derivati piridin-2-il tieno[2,3-d]pirimidina. Na žalost, sa svega dva predstavnika pomenutog strukturnog tipa objektivni zaključak ne možemo izvesti. Planiramo da naša istraživanja posvetimo detaljnijem proučavanju antioksidativnog potencijala 2-supstituisanih piridin-2-il tieno[2,3-d]pirimidina i u ovom kontekstu ćemo i nastaviti sa daljim radom.

Literatura

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IN VITRO ASSESSMENT OF ANTIOXIDANT ACTIVITY OF TETRAHYDRO-BENZO[4,5]THIENO[2,3-D]PYRIMIDINES

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Oxidative stress is involved in numerous pathological states including inflammation, atherosclerosis, diabetes, cancer, neurodegenerative disorders, cardiovascular disorders and other chronic conditions (1). For over three decades numerous studies have highlighted the health benefits of antioxidants and their role in the prevention and treatment of diseases resulting from oxidative damage (2). Thieno[2,3-d]pyrimidine derivatives display a wide range of biological activities such as anti-tumor, anti-inflammatory, anti-diabetic that could be all strongly related to the antioxidant activity interplay. The *in vitro* antioxidant properties of already synthesized and characterized compounds: eleven thieno[2,3-d]pyrimidine-4-amines (3) and six thieno[2,3-d]pyrimidine-4-phthalimides (4) by using lipid peroxidation method were evaluated in order to assess their capacity. The obtained results indicated that among tested thieno[2,3-d]pyrimidines only two compounds 2-(pyridin-2-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-amine (compound 11) and 2-(2-(pyridin-2-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-yl)isoindoline-1,3-dione (compound 17) exhibit antioxidant properties, having $IC_{50} = 90 \pm 4 \mu M$ and $IC_{50} = 165 \pm 40 \mu M$, respectively. However, none of the compounds demonstrated antioxidant activity comparable to that of standard antioxidants, Trolox, caffeic acid and quercetin. A common structural feature of both compounds exhibiting inhibition of lipid peroxidation, compared to other compounds involved in this study, is the 2-substituted pyridin-2-yl thieno[2,3-d]pyrimidine core. Before reaching a firm conclusion, larger number of thieno[2,3-d]pyrimidine-4-amines and thieno[2,3-d]pyrimidine-4-phthalimides with pyridinyl moieties should be included, and in this context we will continue to expand our research in future.

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