Arh. farm 2023; 73: S89–S90 ***PP 29***

ISPITIVANJE ANTIBAKTERIJSKE AKTIVNOSTI SINTETISANIH DERIVATA HALKONA I *IN SILICO* PREDIKCIJE NJIHOVOG FARMAKOKINETIČKOG I TOKSIKOLOŠKOG PROFILA

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Halkoni su biosintetski prekursori sekundarnih metabolita biljaka cvetnica i predstavljaju važnu sintetsku sirovinu i centralne intermedijere u sintezi bioaktivnih heterocikličnih jedinjenja. Halkonski strukturni tip je jednako interesantan i sa aspekta biološke aktivnosti jer ovu klasu jedinjenja karakteriše veliki terapijski potencijal (1). Globalni problem današnjice u lečenju svih vrsta infekcija predstavlja sve veća ekspanzija multirezistentnih patogenih sojeva mikroorganizama. Toksičnost prirodnih biljnih proizvoda na organizme kičmenjaka je mala, kao i mogućnost razvoja rezistencije mikroorganizma nakon dugotrajne primene, što im daje izvesnu prednost u odnosu na konvencionalne terapijske metode. U brojnim istraživanjima potvrđeno je antibakterijsko, antifungalno i antivirusno dejstvo različitih derivata halkona, što ova jedinjenja čini odličnim kandidatima za studije usmerene ka pronalaženju novih antimikrobnih lekova (2). U ovom istraživanju izvršena je sinteza sedam halkonskih derivata Klajzen-Šmitovom aldolnom kondenzacijom iz acetofenona i supstituisanih benzaldehida. Preliminarno ispitivanje antimikrobne aktivnosti sintetisanih derivata izvršeno je mikro-dilucijonom metodom na dva laboratorijski kontrolisana bakterijska soja: *Escherichia coli* i *Staphylococcus aureus*. U testiranoj koncentraciji (1 mg mL^{-1}), 3-bromo-4-hidroksi-5-metoksihalkon i 4,5-dimetoksi-2-nitrohalkon su ispoljili izraženu aktivnost prema *Staphylococcus aureus*-u. U *in silico* sudiji izvedenoj primenom SwissADME platforme i Osiris Property Explorer alata, za aktivna jedinjenja predviđene su povoljne fizičko-hemijske osobine, visoka gastrointestinalna apsorpcija, odsustvo rizika za mutagene, tumorogene, iritirajuće i štetne efekte za reproduktivni sistem, tako da ova jedinjenja mogu predstavljati dobru polaznu osnovu za razvoj potencijalnih antistafilokoknih agenasa.

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Zahvalnica

Rad je finansiralo Ministarstvo nauke, tehnološkog razvoja i inovacija Republike Srbije (Projekat 451-03-47/2023-01/200113) i Medicinski fakultet Univerzitet u Nišu, interni projekat broj 40.

EVALUATION OF ANTIBACTERIAL ACTIVITIES OF SYNTHETIC CHALCONE DERIVATIVES AND *IN SILICO* PREDICTIONS OF THEIR PHAMACOKINETIC AND TOXICOLOGICAL PROFILE

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Chalcones are biosynthetic precursors of secondary metabolites of flowering plants and they represent an important synthetic feedstock and intermediate in synthesis of bioactive heterocyclic compounds. The chalcone structural type is equally interesting in terms of biological activity, so this class of compounds is characterized by great therapeutic potential (1). A trend of increasing expansion of multiresistant pathogenic strains of microorganisms represents the global problem in the treatment of all types of infections. Toxicity of natural products to vertebrates is low, as is the possibility of developing resistance of microorganisms after long-term administration, which represents some advantage over conventional therapeutic methods. Numerous studies have confirmed the antibacterial, antifungal and antiviral effects of various chalcone derivatives, making these compounds excellent candidates for studies aimed at finding new antimicrobials (2). In this research, seven chalcone derivatives were synthesized according to the Claisen-Schmidt condensation method and a preliminary test of the antimicrobial activity of the synthesized derivatives by micro-dilution method was performed on two laboratory-controlled bacterial strains: *Escherichia coli* and *Staphylococcus aureus*. In tested concentration (1 mg mL^{-1}), 3-bromo-4-hydroxy-5-methoxychalcone and 4,5-dimethoxy-2-nitrochalcone exhibited pronounced activity towards *Staphylococcus aureus*. In an *in silico* study which was performed using SwissADME platform and Osiris Property Explorer tool, active compounds were predicted to have favourable physicochemical properties, high gastrointestinal absorption, to pose no risk for mutagenic, tumorogenic, irritating, and reproductive effects. Therefore, they may be considered as good starting point for the development of potential antistaphylococcal agents.

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Acknowledgements

The work was funded by the Ministry of Science, Technological Development and Innovation Republic of Serbia (Project 451-03-47/2023-01/200113) and Faculty of Medicine, University of Niš Internal project No. 40.