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Proučavanje kristalne strukture i interakcija 5-(3- i 4-supstituisanih)-5-metilhidantoina sa albuminom humanog seruma i DNK

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U okviru proučavanja uticaja strukture na farmakološku aktivnost derivata hidantoina, 5-(3-metilfenil)-5-metilhidantoin (**1**) i 5-(4-metoksifenil)-5-metilhidantoin (**2**) su sintetisani i potpuno strukturno okarakterisani određivanjem temperature topljenje, FTIR, ^{1}H i ^{13}C NMR spektroskopskim metodama. Određene su njihove kristalne strukture i izvršena je analiza kristalnog pakovanja sa aspekta međumolekulskih interakcija i strukturnih motiva. U kristalnom pakovanju oba jedinjenja uspostavljaju se jake intermolekulske N-H···O vodonične veze između njihovih *R* i *S* izomera. Vezivanje proučavanih jedinjenja za DNK i serum humanog albumina (HSA) proučavano je merenjem gašenja fluerescencije triptofana. Pokazano je da **2** ima viši afinitet vezivanja i za DNK i HSA od **1**. Predstavljeno istraživanje pruža smernice za dizajniranje novih derivata hidantoina sa poboljšanim farmakološkim svojstvima.

Study of the crystal structure and interactions of 5-(3- and 4-substituted)-5-methylhydantoins with human serum albumin and DNA

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Within the framework of the investigation of the structure–activity relationship of hydantoin derivatives, 5-(3-methylphenyl)-5-methylhydantoin (**1**) and 5-(4-methoxyphenyl)-5-methylhydantoin (**2**) were synthesized and structurally characterized by determination of their melting points, FTIR, ^{1}H and ^{13}C spectroscopic techniques. Their crystal structures were determined and the analysis of the crystal packings in terms of the contributing intermolecular interactions and structural motifs was performed. In the crystal packing of both compounds, strong intermolecular N-H···O hydrogen bonds were observed between their *R* and *S* isomers. Binding of the investigated compounds to DNA and to human serum albumin (HSA) was studied by measuring quenching of the fluorescence of tryptophan. It was shown that **2** has a higher binding affinity for both DNA and HSA than **1**. The presented investigation provide guidance for design of novel hydantoin derivatives with improved pharmacological properties.