CHALCONES ARE POTENTIAL INHIBITORS OF HIV-1 PROTEASE

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The discovery of HIV and the study of molecular mechanisms crucial for the virus replication cycle have led to the identification of important protein structures - potential targets of drug action in AIDS therapy. One of the most significant discoveries is HIV-1 protease (PR), an enzyme that plays a key role in the HIV replication cycle (1). This study aimed to test and demonstrate the interactions of newly synthesized chalcones (1,3-diaryl-2-propen-1-one) as well as three commercial drugs (lopinavir, ritonavir and darunavir) in the active site of HIV-1 protease using *in sillico* methods. and that the results obtained correlate with the results of *in vitro* tests on the enzyme itself. The twenty structurally similar chalcone derivatives were synthesized and their physico-chemical characterization was performed. Docking calculations were performed using the *Autodock Wine* program in the 3D structure of the enzime catalytic site (pdb code: 6B36). The inhibition of enzyme activity was monitored by fluorimetric method (2). The obtained results revealed that all compounds showed anti-HIV-1 protease activity. Compound C1 showed the highest inhibitory activity with an IC_{50} values of 0.001 μM which is comparable with commercial product Darunavir. The results obtained indicate that the synthesized compounds can be classified as potential anti-HIV-1 protease inhibitors. Further research is focused on testing the ADMET properties of the synthesized compounds as well as the synthesis of their analogues for which *in silico* tests have shown satisfactory results.

References

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HALKONI POTENCIJALNI INHIBITORI HIV-1 PROTEAZE

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Otkriće HIV-a i istraživanje molekularnih mehanizama ključnih za ciklus replikacije virusa dovelo je do identifikacije važnih proteinskih struktura - potencijalnih ciljnih mesta dejstva lekova u terapiji AIDS-a. Jedno od najznačajnijih otkrića je HIV-1 proteaza (PR), enzim koji ima ključnu ulogu u ciklusu replikacije HIV-a (1). Ova studija imala je za cilj da primenom *in sillico* metoda ispita i prikaže interakcije novosintetisanih halkona (1,3-diaril-2-propen-1-ona) kao i tri komercijalna leka (lopinavira, ritonavira i darunavira) u aktivnom mestu HIV-1 proteaze i da dobijene rezultate koreliše sa rezultatima *in vitro* testova na samom enzimu. Sintetisano je dvadeset strukturno sličnih derivata halkona i izvršena njihova fizičko-hemijska karakterizacija. *Docking* studije izvedene su u programu *Autodock Vine* u 3D strukturi enzimskog katalitičkog mesta (pdb kod: 6B36). Inhibicija enzimske aktivnosti određena je primenom fluorimetrijske metode (2). Dobijeni rezultati ukazuju da svih 20 jedinjenja ispoljava anti-HIV-1 proteaznu aktivnost. Jedinjenje HNT1 je pokazalo najveću inhibitornu aktivnost sa vrednostima IC50 od 0,001 μM što je uporedivo sa komercijalnim proizvodom darunavirom. Dobijeni rezultati ukazuju da se sitetisana jedinjenja mogu klasifikovati kao potencijalni anti-HIV-1 proteazni inhibitori. Dalje istraživanje je usmereno na ispitivanju ADMET osobina sintetisanih jedinjenja kao i sintezi njihovih analoga za koje su *in silico* ispitivanja pokazala zadovoljavajuće rezultate.

References

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