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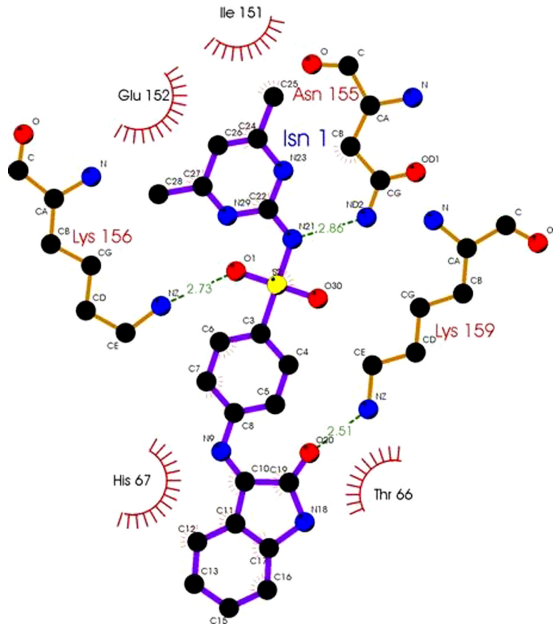
Design, Molecular Modelling Studies on Isatin Analogues as Novel Inhibitors of HIV Integrase

P. Selvam[1,*], M. Chandramohan[2], N. Saravanan Prabhu[3], M. Suresh Kumar[3]

[1] *Devaki Amma Memorial College of Pharmacy, Chelembra, Malapuram, Kerala, India;* [2] *Bharat Ratna Kamarajar Liver Hospital and Research Centre, Madurai 625020, India;* [3] *Centre for Bioinformatics, School of Life Sciences, Pondicherry University, Puducherry 605014, India*

HIV is a member of lentivirus genus, which belongs to retrovirus family and it is single-stranded, positive-sense, enveloped RNA virus leads to the most dreadful disease AIDS. Reverse transcriptase, integrase and protease are the three enzymes which are used as a drug target for the HIV treatment. Among these targets, HIV integrase is the enzyme responsible for integration of viral DNA into the host genome, which is the essential step for viral genome replication. We have synthesized a series of five novel isatin derivatives, which possesses anti-HIV activity identified by the in vitro enzyme inhibition study on HIV integrase. Among them, SPIII-5H possesses highest activity with least IC50 value of 3 μM. In this work, we have predicted the binding modes of isatin derivatives onto the active site of HIV integrase using Glide 5. This docking study shows that critical viral DNA substrate binding residues such as Lys156, Lys159 and Asn155 donates hydrogen bond to compound the active site residues such as Glu 152, Thr66, Ile 151 form hydrophobic interactions. These interactions contribute inhibition activity to the compounds and they share common pharmacophoric features with each other and with available inhibitor 5CITEP. Therefore in this work we propose the pharmacophoric features and bioactive conformation of isatin derivatives and can be used as drug lead for drug designing purpose in the future.



doi:10.1016/j.antiviral.2010.02.406

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Activity of Isatine-sulphadimidine Derivatives Against 2009 Pandemic H1N1 Influenza Virus in Cell Culture

Periyasamy Selvam[1,*], Markandavel Chandramohan[2], Brett L. Hurst[3], Donald F. Smee[3]

[1] *Devaki Amma Memorial College of Pharmacy, Malapuram, India;* [2] *Bharat Ratna Kamarajar Liver Hospital and Research Centre, Madurai, India;* [3] *Institute for Antiviral Research, Utah State University, Utah, USA*

Background: The development of antiviral drugs has provided crucial new means to mitigate or relieve the debilitating effects of many viral pathogens. New classes of inhibitors are essential to combat swine influenza viral infection.

Methods: A series of isatine-sulphadimidine derivatives were screened for antiviral activity against swine influenza A/California/07/2009 (H1N1) virus in MDCK cell culture. Cytotoxicity of the synthesized compounds was also tested in uninfected MDCK cells.

Results: All the compounds inhibit the influenza A (H1N1) in MDCK cells. The most active compounds, SPIII-5Br and SPIII-5H, inhibited virus-induced cytopathology by 50% at 27 and 30 μM, respectively, with 50% cytotoxicity occurring at a much higher dose (975–1000 μM). The positive control compound ribavirin inhibits the replication of the virus at 18 μM and cytotoxic concentration was found to be >1000 μM.

Conclusions: SPIII-5Br and SPIII-5H exhibited potency in the same range as ribavirin, and are suitable candidate molecules for further investigation.

Acknowledgement: The anti-influenza experiments were performed at Utah State University under contractNO1-AI-30048 from the Virology Branch, NIAID, NIH.

doi:10.1016/j.antiviral.2010.02.407

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Studies of HIV Integrase Inhibitory Activity of *Morinda citrifolia* L Noni Fruit Extracts

Periyasamy Selvam[1,*], Kasthuraiah Maddali[2], Christophe Marchand[2], Yves Pommier[2]

[1] *Devaki Amma Memorial College of Pharmacy, Malapuram 676364, India;* [2] *Laboratory of Molecular Pharmacology, National Cancer Institute, Bethesda, MD 20892, USA*

Background: The development of antiviral drugs has provided crucial new means to mitigate or relieve the debilitating effects of many viral pathogens. A rich source for the discovery of new HIV infection inhibitors has been and continues to be, the 'mining' of the large diversity of compounds already available in nature and specifically those from botanical extracts. *Morinda citrifolia* is used in the Indian system of medicine for the treatment of variety of diseases including HIV/AIDS and enriched with flavinoids, anthroquinone and glycoside, but activity against HIV integrase not yet been studied, based on this fact present work is to study HIV integrase inhibitory activity of different extracts of *Morinda citrifolia*.

Method: *Morinda citrifolia* (MC) fruit extracts have been studied against inhibition of HIV-1 integrase enzymatic activity. All extracts of *Morinda citrifolia* were investigated for both 3′ processing and strand transfer process of HIV-1 integrase enzymatic activity.

Results: All extracts exhibited significant inhibitory activity against HIV-1 integrase enzyme (3′P 0.031–24 μg/ml. and ST 0.02–18 μg/ml). The acetone extract (AWT) displayed potent