Viroporins as a potential target of antiviral drugs based on pyrazine derivatives of amino acid esters

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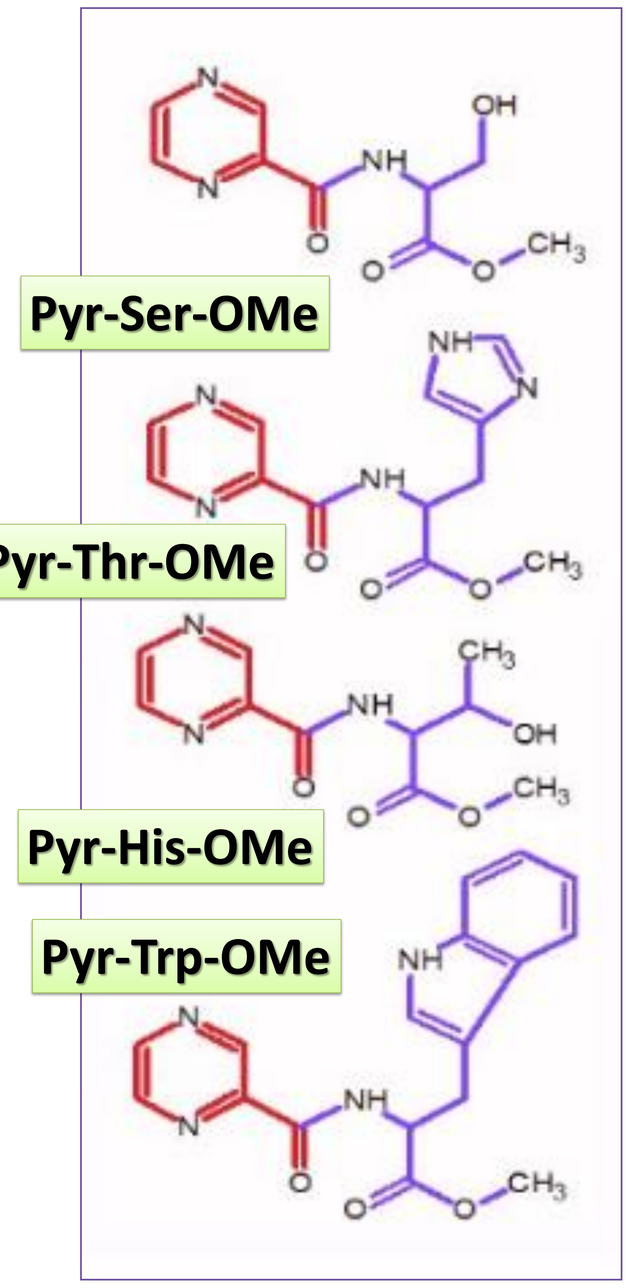
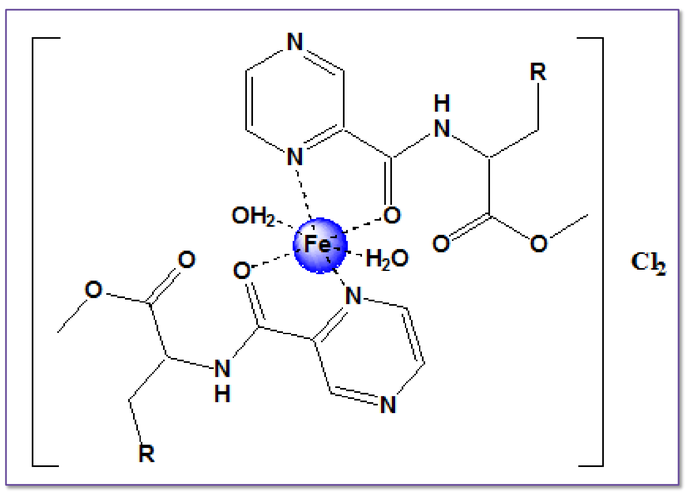
Derivatives of pyrazine-2-carboxylic acid with amino acid esters containing an aromatic and aliphatic side groups were successfully synthesized. In biological experiments in vitro, the target compounds were used as complexes with iron(II) chloride formed in situ at the Fe : L = 1 : 2 ratio to give transparent colorless water solutions. Their antiviral activity against influenza A/H1N1 and SARS-CoV-2 viruses in vitro was studied. Using the MDCK cell culture, it was shown that only **Pyr-Trp-OMe** has the ability to suppress the replication of the pandemic strain of influenza A virus. On the other hand, these compounds were found to have no antiviral properties against the modern strain of coronavirus SARS-CoV-2 in in vitro experiments.



Synthesis of key Fe(II) complexes with Pyr-derivatives

$FeCl_2 + 2L$

H_2O

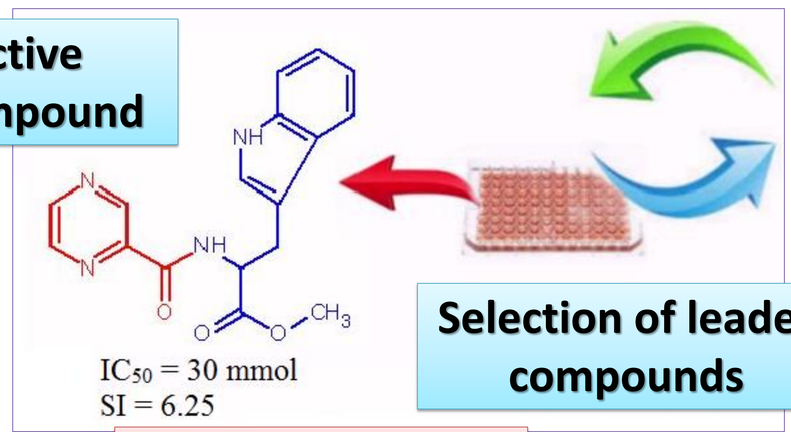


Resistance to existing drugs

Modification of existing drugs

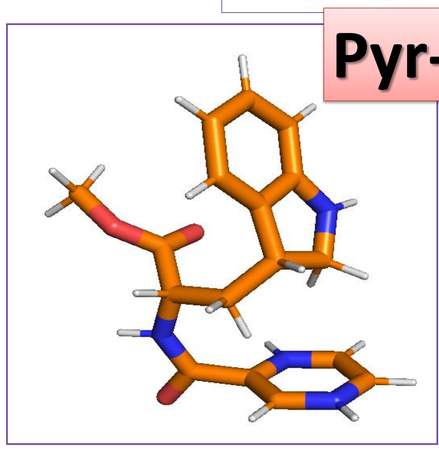
New effective inhibitor compound

Screening of existing structural analogs

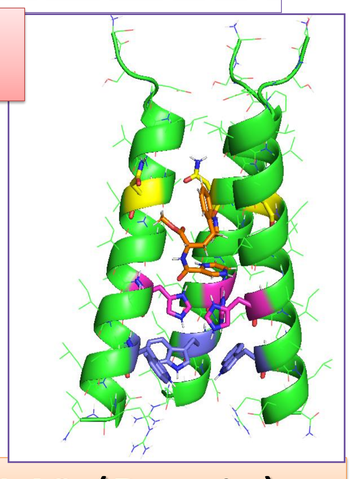


Antiviral activity of compounds **1**–**4** coordinated by iron(II) chloride (in a metal-to-ligand ratio of 1 : 2) against influenza virus strain A/IIV-Orenburg/83/2012(H1N1)pdm09

Compounds	Suppression of viral activity by compounds at various concentrations (%)	
	15 mmol	30 mmol
1 + $FeCl_2$	1.5	19,0
2 + $FeCl_2$	0	31,0
3 + $FeCl_2$	0	20,0
4 + $FeCl_2$	**19.0**	**71.0**
Rimantadine hydrochloride	0	1.5
$FeCl_2$ (2 ligand equivalents, solution in water)	0	0



Pyr-Trp-OMe



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