with the membrane dye octadecyl rhodamine chloride (R18) were exposed to dUY11, and then mixed with Vero cells on ice. Fusion, induced by raising the temperature to 37 °C and lowering the pH to 5.5, was monitored by fluorescence dequenching. Fluorescence was dequenched by 15% when virions were exposed to vehicle, but by only 2.5% when they were exposed to dUY11. Furthermore, inhibition of lipid mixing and infectivity were most consistent for several RAFIs (Table 1). In conclusion, RAFIs inhibit the infectivity of enveloped viruses by targeting virion envelope lipids to prevent fusion of viral and cellular membranes.

	dUY11 (μM)	aUY11 (μM)	aUY12 (μM)	dUY5 (μM)
Fusion IC_{50}	0.0111	0.0149	5.1	3.2
Plaquing IC_{50}	0.0087	0.0096	3.6	3.2

doi:10.1016/j.antiviral.2011.03.029

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Combine Action Rimantadine and Amizon on Flu Occasion

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Last year (ICAR 2010) we have shown that addition antiflogistic to viral inhibitor in vitro potentiated its activity. As next step we treated in vivo flu virus A/H1N1 with simultaneous use rimantadine and amizon (mol: mol). In this case LD_{50} 1500 mg/kg.

Flu virus in dose 10 LD_{50} was applicated mice in a nose. In 1 h rimantadine and amizon in dose 4 mg/ml in 0.2 ml physiology solution was injected intraperitoneally.

Results are below.

Remedy	Mice survival, %	
	After 5 days	After 14 days
Rimantadine	60	60
Amizon 60	40	
Rim. + Am.	100	80
Tamiflu	80	70
Control	0	0

Combine action rimantadine and amizon is more potent on flu occasion in mice.

doi:10.1016/j.antiviral.2011.03.030

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An Analogue of the Antibiotic Teicoplanin Inhibits Dengue Virus Entry *In Vitro*

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The dengue virus is a mosquito-borne virus that belongs to the family of the *Flaviviridae*; it is endemic in (sub) tropical regions. Each year over 50–100 million people become infected with the virus of which about 250,000–500,000 may develop severe and potentially life-threatening conditions, i.e. dengue hemorrhagic fever and dengue shock syndrome. There is neither vaccine, nor therapy available. Here, we report on an analogue of the antibiotic teicoplanin LCTA-949 [devoid of antibacterial activity] that inhibits virus induced CPE in a dose dependent manner (EC_{50} of ~5 μM). This finding is corroborated by the quantification of viral RNA levels in culture supernatant by RT-qPCR (EC_{50} = 4.8 μM). A selectivity index (50% effective concentration/50% cytostatic concentration) of approximately 10 was calculated. Antiviral activity is also observed against other flaviviruses, i.e. the yellow fever virus 17D and the Modoc virus, as well as against the hepacivirus HCV. Time of addition experiments indicate that LCTA-949 inhibits the early stages in the viral lifecycle. This is corroborated by the fact that LCTA-949 lacks activity on DENV subgenomic replicon (that does not contain the structural genes) replication. In addition, in single-virus tracking assays LCTA-949 was shown to inhibit the fusion process. Studies are currently ongoing to unravel the precise mechanism by which LCTA-949 inhibits DENV replication. Insight in the mechanism of action may also shed new light on the early stages of the DENV replication cycle.

doi:10.1016/j.antiviral.2011.03.031

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Identification of HIV-1 Reverse Transcriptase Dual Inhibitors by a Combined Shape-, 2D-Fingerprint- and Pharmacophore-based Virtual Screening Approach

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The human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) is still one of the most attractive targets in the design of new antiviral agents. It is a key enzyme for viral replication which has two associated catalytic functions: a DNA polymerase activity and a ribonuclease H (RNase H) activity. Even though there are several known inhibitors of the RT-associated DNA polymerase function, only few inhibitors of its RNase H function have been identified so far. Here, we report the first application of virtual screening (VS) methods for discovering new inhibitors of this novel and challenging target. The overall VS campaign consisted of two consecutive screening processes, each of it resulting in a hit list of compounds which were tested experimentally. Firstly, the virtual screening platform ROCS (Rapid Overlay of Chemical Structures) was utilized to perform *in silico* shape-based similarity screening in which an hydrazone derivative, previously shown to inhibit the HIV-1 RNase H, was chosen as a query. Consequently, the most active molecules identified in the first VS were selected as queries for a parallel VS which combined three different LB methods: shape-based, 2D-fingerprint, 3D-pharmacophore VS. The effect of the VS selected molecules on the HIV-1 RT-associated activities was evaluated in biochemical assays. Overall, a set of molecules characterized by different scaffolds were identified as new inhibitors of both RT-associated activities in the micromolar range.

doi:10.1016/j.antiviral.2011.03.032