Sudha Srivastava, J Antivir Antiretrovir 2014, 6:2
http://dx.doi.org/10.4172/1948-5964.S1.022

OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Virology

October 06-08, 2014 Hilton San Antonio Airport, TX, USA

Design of novel, potent neuraminidase inhibitor for H5N1 avian influenza using molecular docking, multinuclear NMR and DSC methods

Sudha Srivastava
India

Oseltamivir phosphate is the first orally active neuraminidase (NA) inhibitor approved for the treatment of influenza A and B infections. However, it is not as effective against the neuraminidase subtype N1 as it is against subtypes N2 and N9. It is known that the resistance of neuraminidase subtype N1 to the drug is because the side chains of Glu119 and Asp151 may not have the precise alignment required to bind the oseltamivir tightly. Therefore, it is important to understand the interaction of oseltamivir at the molecular level with the virus, the cell membrane and the enzyme in order to generate ideas that can help modify the drug. In the present study, we have used molecular docking to explore the active site of the enzyme and provide clues for favorable binding interaction that can be used to modify oseltamivir. Based on the results, derivatives with varying charge and lipophilicity have been prepared, by substituting groups at the amino position of oseltamivir to provide additional interaction with the 150-cavity, a well known active site in the neuraminidase subtype N1. To understand the effect of these groups on the binding of the derivatives to the enzyme, the parent compound and its derivatives were docked into the enzyme H5N1-NA active site and their binding energies analyzed.

Further, to predict their drug effectiveness, the interaction of these derivatives with model membranes and the effect on the thermotropic behaviour and polymorphism of the membrane bilayers has been investigated by NMR, DSC and TEM methods A comparison of four potential inhibitors with oseltamivir indicates that the glycyl derivative of oseltamivir has the most profound effects on the membrane, compared to the other derivatives. It seems to be the most promising derivative for further pharmacological evaluation as a neuraminidase inhibitor.

Biography

Sudha Srivastva's main research interest is drug design using molecular modeling, molecular docking, NMR, DSC and TEM techniques. She has extensively used two-dimensional NMR technique to obtain distance constraints to carry out ligand-receptor interaction studies. Her current research interest is designing of neuraminidase inhibitors using structure-based drug design. Other areas of her research interests are: protein conformation, membrane architecture, and metabolomics. She is Fellow of National Academy of Sciences, India. She has published more than 116 papers in journals of international repute.

sudha@tifr.res.in