

virus-stimulated JNK phosphorylation, on a dose-dependent manner. Furthermore, at 40  $\mu$ M, a concentration where  $\geq 90$  of the cells were viable, virus replication was significantly reduced, with the decline in virus yields reaching from  $\geq 90$  to 99%, depending on the infected cell line (A31, BSC-40 or BHK-21). The decline in virus titers was followed by an arrest verified in the transition from immature virus (IV) to intracellular mature virus (IMV) stage of the morphogenic cycle. Despite the fact that SP600125 can act as an efficient anti-poxviral compound, we also provide evidence that this antiviral effect is not specifically exerted through JNK1/2 inhibition. This conclusion is supported by the fact that viral titers measured after infections of JNK1/2 Knock-out cells were not altered as compared to those obtained from infected-wild-type cells. In contrast, a decline in viral titers was verified when the infection of KO cells was carried out in the presence of the pharmacological inhibitor. SP600125 has been the focus of recent studies that have evaluated its action on diverse viral infections including DNA viruses of *herpesviridae* family. Our data support the notion that SP600125 can be regarded as a potential anti-poxviral compound.

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69

#### Anti-viral Properties and Mode of Action of Standardized *Echinacea purpurea* Extract Against Highly Pathogenic Avian Influenza Virus (H5N1, H7N7) and Swine-origin H1N1 (S-OIV)

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Influenza virus (IV) infections are a major threat to human welfare and animal health worldwide. Anti-viral therapy includes vaccines and a few anti-viral drugs. However vaccines are not always available in time, as demonstrated by the emergence of the new 2009 H1N1-type pandemic strain of swine origin (S-OIV) in April 2009, and the acquisition of resistance to neuraminidase inhibitors such as Tamiflu® (oseltamivir) is a potential problem. Therefore the prospects for the control of IV by existing anti-viral drugs are limited. As an alternative approach to the common antivirals we studied in more detail a commercial standardized extract of the widely used herb *Echinacea purpurea* (Echinaforce®, EF) in order to elucidate the nature of its anti-IV activity. Human H1N1-type IV, highly pathogenic avian IV (HPAIV) of the H5- and H7-types, as well as swine origin IV (S-OIV, H1N1), were all inactivated in cell culture assays by the EF preparation at concentrations several orders of magnitude below the recommended dose for oral consumption. Detailed studies with the H5N1 HPAIV strain indicated that direct contact between EF and virus was required, prior to infection, in order to obtain maximum inhibition in virus replication. Hemagglutination assays showed that the extract inhibited the receptor binding activity of the virus, suggesting that the extract interferes with the viral entry into cells. In sequential passage studies under treatment in cell culture with the H5N1 virus no EF-resistant variants emerged, in contrast to Tamiflu®, which produced resistant viruses upon passaging. Furthermore, the Tamiflu®-resistant virus was just as susceptible to EF as the wild type virus.

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70

#### Novel Chemical Compounds as Potential Blockers to the Swine-Origin Influenza A H1N1 (2009) Virus Replication

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**Background:** The swine-origin influenza A H1N1 (2009) virus, identified in late March 2009 in Mexico, had a brutal impact. Moreover, the lack of effective antiviral therapies against the virus assisted in its progress to cause a pandemic. The increasing capability of the influenza A viruses to develop resistance against antiviral drugs is posing a severe problem in the prophylactic measures for the virus control. Thus, new antiviral drugs are required for control of influenza virus infections.

**Methodology:** In our study, we analyzed the activity of two novel chemical compounds (kindly provided by Dr. Prasad, Department of Chemistry, University of Delhi) against the seasonal and pandemic influenza A viruses both *in vitro* (MDCK cell line) and *in vivo* (Balb/c mice). The cells and mice were infected with influenza virus strains separately and treated with the compounds, code names: CP1 and CP2. The percentage protection offered by these compounds was determined by MTT assay (*in vitro*) and survival assay (*in vivo*). The degree of virus inhibition by these novel compounds was also analyzed by viral plaque assay, real time RT PCR and Western blotting.

**Results and conclusion:** Percentage viability of the cells, after treatment with the compounds, increased by 54% and 47% in the presence of CP1 and CP2 respectively. *In vitro* experiments exhibited up to 50% inhibition of the viruses. Approx. 40% inhibition of viral gene expression was also observed in the *in vivo* studies using Balb/c mice. Hence, the two new compounds tested by us may prove as effective antiviral measures for prophylaxis and treatment of infections resulting from the seasonal and/or emerging strains of the influenza virus.

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71

#### Photodynamic Effect of Phthalocyanine-Zn (II) Complexes on Some Enveloped Viruses

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**Objective:** Various phthalocyanines have been studied for their capacity for photodynamic inactivation of viruses. Two new water-soluble phthalocyanine-Zn (II) complexes with different charges – cationic methylpyridyloxy-phthalocyanine (ZnPcMe) and anionic sulfophenoxy-phthalocyanine (ZnPcS), were used for photoinactivation of two DNA viruses, herpes simplex virus type 1 (HSV-1) and vaccinia virus (VV), and two RNA containing enveloped viruses: bovine diarrhoea virus (BVDV) and Newcastle disease virus (NDV).

**Experimental design:** Aliquots of 0.1 ml stock virus were mixed with 0.1 ml solution containing 0.58  $\mu$ M ZnPcMe or 0.64  $\mu$ M ZnPcS. The mixtures were irradiated for 5 and 20 min at room temperature by fluence rate 100 mW cm<sup>-2</sup> controlled by the photometer