Tamiflu Metabolite Found in Sewage Discharge, River Water

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(PhysOrg.com) -- In a study published September 28th ahead of print in the peer-reviewed journal *Environmental Health Perspectives*, researchers measured oseltamivir carboxylate (OC), the active metabolite of the popular anti-influenza drug Tamiflu (oseltamivir phosphate), in samples of sewage discharge and river water collected near Kyoto City during Japan's 2008-2009 flu season.

Scientists already knew that OC withstands the activated sludge treatment process used by many sewage treatment plants (STPs) and that the metabolite is released in STP wastewater, but the amount of OC reaching waterways as a result of this had not been measured. Therefore, the goal of the current study was to assess differences in the occurrence of OC in these waters over the course of a seasonal flu outbreak.

OC concentrations were highest in all samples during the peak of the seasonal flu outbreak, with the highest concentration, 293.3 nanograms per liter (ng/L), measured in discharge water from a conventional activated sludge-based STP. However, OC levels in discharge samples varied significantly depending on the type of sewage treatment method used, with a substantially lower peak concentration (37.9 ng/L) measured in discharge from an STP that used ozonation as an additional (tertiary) treatment.

The points where treated effluent is discharged into waterways tend to be warmer and resist freezing in winter, making them attractive spots for wild waterfowl. When influenza A virus in the birds' droppings

encounters active Tamiflu metabolite in the water, the scene is set for resistance to develop.

Previous studies have reported that the concentrations of OC required to disable 50% of influenza virus—a measure of the drug's effectiveness—ranged from 80 to 230 ng/L. Thus, the peak drug concentrations observed in this study may be high enough to promote the emergence of drug-resistant influenza strains in waterfowl exposed to OC-contaminated waterways.

Seasonal flu epidemics cause tens of millions of respiratory illnesses and 250,000 to 500,000 deaths worldwide each year, according to the World Health Organization (WHO). The WHO recommends Tamiflu for both treatment and prevention of flu, and the drug is considered an important first-line defense in the event of a flu pandemic, including the current pandemic of H1N1 flu. However, there are widespread reports of resistance to Tamiflu among seasonal influenza. A growing number of similar reports in regards to novel H1N1 influenza highlight the need for measures to control the emergence and spread of drug-resistant viral strains.

"Ozonation as tertiary treatment will substantially reduce the OC load in STP effluent during an influenza epidemic or pandemic," wrote first author Gopal C. Ghosh and colleagues. "Further research is needed to investigate the fate of antiviral drugs at every unit process in the STPs."

Other authors of the paper include Norihide Nakada, Naoyuki Yamashita and Hiroaki Tanaka. This study was partially supported by The Ministry of Land, Infrastructure, Transport and Tourism of Japan and the Japan Society for the Promotion of Science.

More information: The article is available free of charge at www.ehponline.org/docs/2009/0900930/abstract.html .