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Oseltamivir Carboxylate – the Active Metabolite of Oseltamivir Phosphate
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Key words: influenza, LC-MS/MS, oseltamivir carboxylate, sewage discharge, Tamiflu, river water.

Abbreviations:

A2O	Anaerobic/Anoxic/Oxic process
AOAO	Anoxic/Oxic/Anoxic/Oxic process
CAS	Conventional Activated Sludge
EMA	European Medicines Agency
HRT	Hydraulic Retention Time
LC	Liquid Chromatography
LOD	Limit of Detection
LOQ	Limit of Quantification
MHLW	Ministry of Health, Labour and Welfare of Japan
MRM	Multiple Reaction Monitoring
MS	Mass Spectrometry
OC	Oseltamivir Carboxylate
OC-D ₃	Oseltamivir Carboxylate labeled with deuterium
OP	Oseltamivir Phosphate
SPE	Solid Phase Extraction
SRT	Sludge Retention Time
STP	Sewage Treatment Plant
WHO	World Health Organization

Outline:

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Abstract

BACKGROUND: Oseltamivir phosphate (OP; Tamiflu) is a prodrug of the anti-influenza neuraminidase inhibitor oseltamivir carboxylate (OC), and has been developed for the treatment and prevention of both A and B strains of influenza. The recent increase in OP resistance in influenza A virus (H1N1) has raised questions about the widespread use of Tamiflu in seasonal epidemics and the potential ecotoxicological risk associated with its use in the event of a pandemic.

OBJECTIVES: (1) To develop an analytical method for quantitative determination of OC in sewage treatment plant (STP) effluent and receiving river water. (2) To investigate the occurrence of OC in STP effluent and river water in Japan during a seasonal flu outbreak.

METHODS: We developed a successful analytical method based on solid-phase extraction followed by liquid chromatography – tandem mass spectrometry. Three sampling campaigns were conducted during the 2008–09 flu season in Kyoto City, Japan.

RESULTS: The highest concentration of OC detected in STP discharge was 293.3 ng/L from a conventional activated-sludge-based STP, but only 37.9 ng/L from an advanced STP with ozonation as a tertiary treatment. In the receiving river water samples, OC was detected in the range of 6.6 to 190 ng/L.

CONCLUSION: OC is present in STP effluent and river water only during the flu season.

Ozonation as tertiary treatment in STP will substantially reduce the OC load in STP effluent during an influenza epidemic or pandemic.