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INFLUENCE OF pH ON AQUATIC TOXICITY OF A MODEL WEAK BASE: A CASE STUDY WITH THE ANTIDEPRESSANT SERTRALINE

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ABSTRACT: Pharmaceuticals are designed with unique physical-chemical properties that may optimize the amount of administered compound reaching target sites within an organism. Many therapeutics reported in surface waters are ionizable compounds; ionization state is strongly influenced by a chemical specific dissociation constant (pKa) and the pH of a biological matrix. Although unionized forms may be more bioavailable due to greater lipophilicity, an integrated understanding of how site specific pH influences aquatic hazards have routinely not been considered in prospective and retrospective ecological risk assessments of ionizable contaminants of emerging concern. This is critical because variations in pH in receiving systems may introduce uncertainty in ecological risk estimations. Sertraline, a selective serotonin reuptake inhibitor that is the most commonly prescribed antidepressant in the United States, was used as a model contaminant to test our hypothesis that ambient pH strongly influences aquatic toxicity of this compound. Sertraline is a weak base with a pKa value (9.27) that approaches the instream pH of the Trinity River, a municipal effluent dominated system in Texas with instream pH greater 8.5. We conducted various bioassays with juvenile Pimephales promelas (fathead minnow) at three environmentally relevant pH levels (6, 7.5 and 9). From three 48-h acute experiments we calculated mean LC50 values of 77, 204, and >500 µg/L for pH 9, 7.5, and 6, respectively. In a time to death study in which fish were exposed to 500 µg/L, 50% mortality was observed after 5 h at pH 9 and 36 h at pH 7.5, whereas survivorship remained 95% at pH 6 even after 48 h. Following a 7 d subchronic study with P. promelas, we also noted a 10-fold difference in No/Lowest Observable Adverse Effects Concentration (NOAEC, LOAEC) for pH 9 compared to pH 6. These findings indicate that sertraline is most bioavailable and most toxic as its unionized:ionized ratio increases. Further, ionization state and site-specific correction factors associated with instream pH may be required to reduce uncertainty in future retrospective and prospective ecological risk assessments of ionizable pharmaceuticals.

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