OZONATION OF RANITIDINE UNDER VARIOUS PHYSICOCHEMICAL CONDITIONS. DEGRADATION KINETICS AND INTERMEDIATE BY-PRODUCTS

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Ranitidine is pharmaceutical compound, widely used for the treatment of ulcer and other gastrointestinal conditions. Its occurrence in surface waters and wastewater has been established. Ozonation can be a useful technique for the degradation of ranitidine in water, since molecular ozone selectively attacks organic compounds with high electron density functional groups, such as double bonds, activated aromatic rings or deprotonated amines. The objectives of this study was to assess the effects of various operational parameters (pH, ozone concentration, presence of hydroxyl radical scavengers, matrix effects and natural organic matter) on the kinetics of the ozonation process and to identify and elucidate the structure of intermediate oxidation by-products of ranitidine in aqueous solutions during the ozonation process. Results proved the high reactivity of ranitidine with molecular aqueous ozone with half-life times ranging 0.3-0.5 min. Reaction kinetics are greatly influenced by the initial ozone concentration, with ranitidine removal higher than 80% observed at initial ozone concentrations above 5 mg L^{-1}. As expected, pH was a significant process parameter, with increased values enhancing degradation kinetics and overall percentage of mineralization. Pseudo-first-order reaction constants ranged 0.19-6.06 min^{-1} and the highest values were observed at lower initial ranitidine concentrations and alkaline solutions. At low pH mineralization was limited, while at pH 10, mineralization reached 68%. Water that included cations and ions such as chlorides, bicarbonates, sodium and calcium, tended to decrease the overall ranitidine removal. NOM acted antagonistically, consuming ozone and limiting its overall degradation. Hydrolysis of ranitidine at different pH was limited and this minimal degradation occurred only in extended time periods (>2 days). Furthermore, the main intermediate byproducts of ozonation degradation were identified and structurally elucidated using liquid chromatography coupled to quadrupole-time-of-flight tandem mass spectrometry (HPLC-QqTOF-MS/MS). After background subtraction, selected chromatographic peaks were analyzed and possible molecular formulas based on their exact m/z values were proposed. MS/MS data in relation to various databases were employed in order to tentatively identify intermediate by-products. Proposed by-products showing lowest error (ppm) and highest identification score (including isotopic pattern), along with their chemical structures, include sulfoxide $C_{13}H_{22}N_4O_4S$, imine $C_{13}H_{21}N_3O_2S$ and nitrocompound $C_4H_{10}N_3O_2$ indicating a direct attack of the molecular ozone to the sulfur and amine group of the compound.

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