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Development of mutagenicity during degradation of N-nitrosamines by advanced oxidation processes

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ABSTRACT

Development of mutagenicity of five *N*-nitrosamines (*N*-nitrosodimethylamine (NDMA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosopyrrolidine (NPYR) and *N*-nitrosodiphenylamine (NDPhA)) was investigated during oxidative processes involving UV-photolysis, ozone and $^{\bullet}$OH radicals. The mutagenicity was detected by the Ames test with 3 different strains, TA98, TAMix and YG7108, a strain which is sensitive for *N*-nitrosamines, in presence and absence of metabolic activation (S9). UV photolysis of mutagenic *N*-nitrosamines (NDMA, NDEA, NDPA and NPYR) leads to the removal of their specific mutagenic activity as detected in YG7108 in the presence of S9. A formation of mutagens during UV photolysis was detected only in case of NDPhA in the strain TA98. Oxidation products of NDMA, NDEA and NDPhA did not show any significant mutagenicity in the strains used, whereas oxidation of NDPA and NPYR by hydroxyl radicals seems to lead to the formation of direct mutagens (mutagenic in the absence of S9) in YG7108 and TAMix. Oxidation by hydroxyl radicals of *N*-nitrosamines with chains longer than ethyl can mimic metabolic activation of *N*-nitrosamines *in vivo*.

1. Introduction

1.1. Occurrence and formation

N-nitrosamines represent an important class of carcinogenic environmental contaminants (Lijinsky and Epstein, 1970). *N*-nitrosamines are formed as byproducts of various manufacturing and natural processes and also occur as disinfection byproducts in water treatment. Their formation during disinfection of drinking water has recently become a great concern (Richardson and Postigo, 2012). In this context, *N*-nitrosodimethylamine (NDMA) is the most prominent representative of this class of compounds. The extent of

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nitrosamines formed depends on the applied disinfection process and the composition of the treated water. Some precursors of oxidative NDMA formation have been identified (Mitch et al., 2003). Chloramination and chlorination are important sources of NDMA, but also alternative treatments, such as ozonation, can lead to formation of *N*-nitrosamines or their precursors (Krasner et al., 2013). Different classes of nitrogenous micropollutants can be precursors for NDMA during chloramine disinfection (Le Roux et al., 2011; Shen and Andrews, 2011). Only a few precursors of NDMA were identified so far for ozonation of waters. An example is dimethylsulfamide, a metabolite of the fungicide tolylfluamide, which leads to NDMA in a bromide-catalyzed reaction (Schmidt and Brauch, 2008; von Gunten et al., 2010), and two semicarbazides in sewage treatment plants (Kosaka et al., 2009).

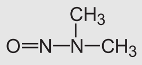
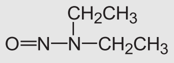
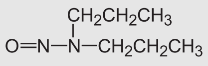
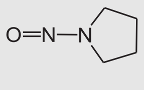
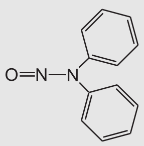
1.2. *Degradation*

N-nitrosamines are not sufficiently abated during common water treatment processes, such as activated carbon adsorption, reverse osmosis or oxidation, but they can be efficiently removed by photolysis (Hrudey and Charrois, 2012). Their prominent photochemical reactivity is favoured by a typical strong absorption band around 230 nm, which is associated with a $\pi \rightarrow \pi^*$ intramolecular charge transfer. They also possess a weaker absorption near 320 nm, corresponding to an $n \rightarrow \pi^*$ electronic transition (Stefan and Bolton, 2002), which is responsible for their degradation under sunlight (Plumlee and Reinhard, 2007). The quantum yields for UV irradiation are quite high (Table 1, (Plumlee and Reinhard, 2007; Sharpless and Linden, 2003)). The photochemical degradation of NDMA during UV irradiation was studied in detail previously (Lee et al., 2005; Plumlee et al., 2008; Stefan and Bolton, 2002). The efficiency of the removal of NDMA depends on the pH, due to protonation of excited NDMA, and on the oxygen concentration due to direct oxidation of excited NDMA by dissolved oxygen (Lee et al., 2005). The degradation products formed by different pathways are amines (e.g. dimethylamine, methylamine, etc.), formaldehyde, formic acid and inorganic compounds such as nitrite and nitrate. Similar degradation products were found under UV and solar light irradiation (Lee et al., 2005; Plumlee and Reinhard, 2007; Stefan and Bolton, 2002). The reactivity of hydroxyl radical (•OH) with the *N*-nitroso group is very low (Landsman et al., 2007; Mezyk et al., 2008, 2004); the rate of oxidation of *N*-nitrosamines by •OH depends strongly on the other functional groups present in their structures. Also, the direct reaction of ozone (O_3) with the *N*-nitroso group or alkyl chain is a very slow process. A higher reactivity of hydroxyl radicals and ozone is expected only for the aromatic ring of NDPhA (von Sonntag and von Gunten, 2012). Consequently, •OH oxidation and ozonation do not seem to be economically feasible for NDMA removal (Lee et al., 2007; Sharpless and Linden, 2003).

1.3. *Toxicity, regulations and testing*

NDMA is the most frequently detected *N*-nitrosamine in drinking water, typically in concentrations <10 ng L^{-1}, but its concentration can exceed 100 ng L^{-1} (Charrois et al., 2004; Zhao et al., 2006). The standard for a lifetime exposure cancer risk of 10^{-5} for drinking water was determined to be 100 ng L^{-1} by the World Health Organisation (WHO, 2008a), in Canada the maximum allowable NDMA concentration is

Table 1 – Photolysis quantum yields and second-order rate constants for the reaction of selected N-nitrosamines with hydroxyl radicals and ozone. Rate constants in bold were determined in this study.

	Chemical structure	Quantum yield	$k_{O3}(M^{-1}\ s^{-1})$	$k_{OH}(M^{-1}\ s^{-1})$
N-nitrosodimethylamine (NDMA) CAS-62-75-9	 $O{=}N{-}N(CH_3){-}CH_3$	0.41^a 0.3^b	0.05 (Lee et al., 2007) **0.02**	4.3×10^8 (Mezyk et al., 2004)
N-nitrosodiethylamine (NDEA) CAS 55-18-5	 $O{=}N{-}N(CH_2CH_3){-}CH_2CH_3$	0.43^a	**0.08**	7×10^8 (Mezyk et al., 2008)
N-nitrosodi-*n*-propylamine (NDPA) CAS 621-64-7	 $O{=}N{-}N(CH_2CH_2CH_3){-}CH_2CH_2CH_3$	0.46^a	**0.04**	2.3×10^9 (Landsman et al., 2007)
N-nitrosopyrrolidine (NPYR) CAS 930-55-2		0.55^a	**0.33**	1.75×10^9 (Landsman et al., 2007)
N-nitrosodiphenylamine (NDPhA) CAS 86-30-6			**8.5**	**6.5×10^9**

[a] $\lambda_{irradiation} > 280$ nm (Plumlee and Reinhard, 2007).
[b] $\lambda_{irradiation} < 300$ nm (Sharpless and Linden, 2003).