Methyl Nitrite as a Significant Public Health Hazard

by

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It has been suggested that MTBE in gasoline will produce methyl nitrite (CH_3ONO) in the exhaust[1]. To date, there have been no attempts to ascertain if this is true or false. However, several university groups with expertise in combustion chemistry consider the idea to be very plausible. Here I review the known toxicology of methyl nitrite, especially as it may relate to the widespread citizen complaints of symptoms attributed to MTBE in gasoline, as well as the huge increase in asthma that has occurred in several cities in which MTBE is used as an oxygenate[2]

Toxicology of Methyl Nitrite and Related Compounds

Methyl nitrite (MN) is one of a class of compounds called alkyl nitrites, with the generalized formula R-O-N-O. MN is the simplest and lightest compound in this class. MN is not available commercially, but is used in certain industrial processes. Higher members of the alkyl nitrite family, including butyl and amyl nitrite, are available and have been widely abused for their neurological effects. For this reason, there is considerably more toxicological data on the higher alkyl nitrites than on MN itself. However, the existing data suggest that, if anything, MN is many times more toxic than butyl or amyl nitrite.

Some of the acute effects of MN are known from animal experiments as well as from accidental industrial exposure to humans. The lethal concentration of MN by inhalation in a four hour exposure to rats is only 170 ppm.[3] This is 100 times less than the corresponding value for benzene, and at least 100 times less than the value for MTBE. In other words, by this test MN is 100 times more toxic than benzene. The cause of death is apparently massive pulmonary hemorrhage. The data also indicate that MN is many times more toxic than the drugs of abuse, butyl and amyl nitrite.

There have been several reports of accidental exposure of industrial workers to MN, resulting in methemoglobinemia sufficiently serious to require immediate hospitalization. Prominent symptoms include headache and heart palpitations.[4,5] These are both very significant for our purpose, since headache was the most common complaint found by the CDC investigations of health problems from MTBE in both Alaska[6] and Connecticut[7]. Furthermore, statistical data from the Philadelphia Department of Health indicate that the number of people treated for cardiac dysrhythmia increased very substantially between 1993 and 1996, the first three years of large scale MTBE usage here.[1]

There are much more data on the abused drugs butyl and amyl nitrite. They are known to depress the function of the immune system in both humans and animals.[8] They can also induce respiratory problems such as tracheobronchitis, cough, and dyspnea[9]. In some cases, people have developed allergic reactions to amyl nitrite.[10] The possibility of

allergy to MN is important because there are reports of people developing true and serious allergic reactions to exhaust from fuel containing MTBE. In general, the toxicity of the alkyl nitrites is sufficiently serious that the U.S. Congress has twice passed laws to make their sale illegal (public laws 100-690: section 2404, and 101-647:section 3202).

MN is known to be mutagenic by the Ames test.[11] This implies, with a probability of about 90%, that it is carcinogenic. The whole question of cancer attributable to nitrites has received considerable attention. There is a very plausible biochemical model that suggests that nitrites may be converted into other compounds, called nitrosamides, which are definitely carcinogenic. There are serious proposals that amyl or butyl nitrite may be the cause of Kaposi's sarcoma, and that the induction of this cancer may be related to suppression of immune function in people who abuse the higher nitrites.[8] It has also been proposed that certain brain tumors in children may be due to *in utero* exposure to nitrosamides stemming from the mother's exposure to nitrites.[12] There are some indications that excessive nitrite (or nitrate) in the food may cause cancer, but most epidemiological studies are inconclusive. Here we want to point out that there are two major differences between MN in the ambient air and nitrites as food additives. First, nitrite in food is invariably inorganic, such as sodium nitrite, which is ionic and water soluble. MN, on the other hand, is fat soluble. Secondly, the mode of entry of MN is via inhalation, rather than oral ingestion. There are many substances that are safe to swallow but are highly toxic when inhaled. Therefore, a failure to demonstrate that inorganic nitrites in food are carcinogenic must not be interpreted to mean that inhaled MN is not carcinogenic. Furthermore, even if inorganic nitrite is eventually shown not to be carcinogenic, the experiments of Tornqvist et al [11] clearly show that the mutagenicity of MN is independent of its conversion to inorganic nitrite, or, as they put it, "the mutagenicity of methyl nitrite is now clear".

Environmental Research in Methyl Nitrite

Environmental scientists have been concerned about MN for many years. MN will be rapidly photolyzed by sunlight, with a mean lifetime of about 10-15 minutes.[13] The result is the production of NOx, which would then contribute to an increase in ozone. This may be a factor to explain why the use of RFG with MTBE has not produced significant reductions in ozone, according to a recent report by the National Research Council.[14]

The fact that methyl nitrite is rapidly destroyed by sunlight explains the "cloudy day" effect, in which sensitive individuals experience symptoms only at night or on dark cloudy days without rain.[15]. Furthermore, by far more asthma attacks occur at night than during the daytime (when ozone concentrations are maximal)[16], so MN may be a very significant factor in asthma attacks that has not been investigated.

In 1982, a Swedish group demonstrated that the addition of methanol to diesel fuel produced small amounts of MN in the exhaust, but they saw none when methanol was added to gasoline[17]. It is known that methanol in gasoline engines does not produce significant quantities of methyl nitrite. This probably explains why many people who suffer various symptoms in regions where MTBE is the oxygenate become asymptomatic

when they travel to regions where only ethanol is used; i.e., the ethers are far more harmful than the alcohols.

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Acute Lethal Toxicities for Various Air Toxics
Smaller LC50 means chemical is more toxic

{PRIVATE }Compound	Species	Duration	LC50:ppm	Source
Formaldehyde	cat	8 hours	650	Patty's-1
Acetaldehyde	rat	4 hours	13,300	Appleman
Benzene	rat	4 hours	16,000	Smyth
1,3,butadiene	rat	*	>> 8,000	Thorton-Manning
MTBE	rat	4 hours?	> 18,000	Costantini
CO	rat	3 hours	2100	Massad
Methanol	cat	4 hours	65,700	Patty's-2
Methyl Nitrite	rat	4 hours	170	Klonne

This table presents the median lethal concentrations for those compounds considered to be "air toxics", as compared with methyl nitrite. In most cases, the end point is death within four hours. This obviously does not address other effects; for example, formaldehyde is irritating at concentrations of several ppm. The table also does not address chronic exposure effects such as cancer, which is induced by 1,3,butadiene at concentrations lower than 8000 ppm. The real issue for us, of course, is public health effects from possible MN in the ambient air. Evidence suggests these are due to some kind of sensitivity reaction on the part of sensitive individuals (humans and perhaps cats). Data on such sensitivities are not available.

* No acute four hour LC50 studies for 1,3,butadiene were found. Chronic studies often use 8000 ppm with no apparent acute effects.

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