ETHANOL: BRIEF REPORT ON ITS USE IN GASOLINE

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MARCH 1, 1999

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**Brief Report on
its Use in Gasoline**

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March 2, 1999

Sponsored by the Renewable Fuels Association

ETHANOL

Introduction

The purpose of this short paper is to summarize information about ethanol's health and environmental effects, given ethanol's use as a fuel oxygenate. The conclusions are: (1) ethanol is readily degraded in the environment; (2) anticipated human exposures to ethanol are very low; and (3) voluminous information on metabolism of ethanol by humans, and on the health effects of ingested ethanol, strongly suggests that environmental exposures to ethanol will have no adverse health impact.

Environmental behavior

Recent reviews of the environmental behavior of gasoline oxygenates generally note that ethanol is not likely to accumulate or persist for long in the environment. For example, the Interagency Assessment of Oxygenated Fuels (NSTC, 1997) observes that ethanol is expected to be rapidly degraded in groundwater and is not expected to persist beyond source areas. Ethanol in surface water is also expected to undergo rapid biodegradation, as long as it is not present in concentrations directly toxic to microorganisms (NSTC, 1997; Malcolm Pirnie, Inc., 1998). The half-life of ethanol in surface water is reported to range from 6.5 to 26 hours (Howard *et al*., 1991). Atmospheric degradation is also predicted to be rapid (Malcom Pirnie, Inc., 1998).

In part, expectations of ethanol's degradability rely on experiments that use microcosms of groundwater and soil mixtures to demonstrate that ethanol is rapidly degraded both aerobically (100 mg/l in 7 days, Corseuil *et al.*, 1998;) and anaerobically (100 mg/l in 3 to 25 days, depending on conditions Corseuil *et al*., 1998; 96 mg/l within 30 days, Suflita and Mormile, 1993; 100 mg/l within 14 days, Yeh and Novak, 1994). In these experiments, ethanol generally delays degradation of BTX, but not always, and some investigators (Corseuil *et al*., 1998) caution against generalizations about ethanol's effect.

Health effects

Ethanol, the active ingredient of alcoholic beverages, has been part of the human diet ‚Äî and the human environment ‚Äî for thousands of years. It is produced by fermentation by fungi and other microorganisms, and is found at low levels in the blood and breath of persons who do not drink alcohol. Biological exposures and responses to ethanol are typically evaluated in terms of the blood concentrations, where the units of concentration are milligrams of ethanol per deciliter of blood, or

mg/dl. Some blood ethanol concentrations (BEC) and associated effects are shown in Table 1. Endogenous blood levels of ethanol range from non-detectable to 0.02 mg/dl to 0.15 mg/dl (Jones, 1985; Lester, 1962). A typical alcoholic beverage contains 12 g of alcohol, corresponds to a dose of about 170 mg/kg for a 70-kg adult, and produces a peak blood ethanol concentration on the order of 25 mg/dl. Legal limits on blood alcohol for drivers of vehicles are typically 80-100 mg/dl.

Ethanol is widely ingested in alcoholic beverages, usually with only mild effects. However, at sufficiently high doses, ethanol can cause toxic effects in humans, both short-term (such as inebriation) and long-term (such as cirrhosis of the liver). If ethanol becomes a common fuel additive, there may be opportunities for exposure by inhalation: ethanol vapors might be inhaled at gasoline stations or in automobiles, for example. Thus, concern has been raised about the possible health consequences of using ethanol for this purpose.

The scientific literature contains virtually no reports of injury to humans from inhaled ethanol. The apparent lack of harm may be attributable to rapid metabolism of ethanol and the difficulty in significantly raising blood ethanol concentrations by inhalation exposure, which keep internal doses extremely low except in unusual situations, such as heavy exercise in the presence of concentrated vapors. The occupational standard for ethanol in air is 1000 ppm (1900 mg/m^3) on an eight-hour basis. The occupational experience with ethanol in air appears to be favorable: no symptoms at levels below 1000 ppm are reported: at this or higher concentrations, ethanol vapor causes eye and upper respiratory tract irritation, fatigue, headache, and sleepiness (ACGIH, 1991; Clayton and Clayton, 1994). No reports regarding chronic exposure of humans to ethanol vapors have been located.

Laboratory animals, chiefly rats, have been subjected to inhalation exposure in a variety of experiments, most investigating aspects of central nervous system or developmental toxicity. The majority of exposures have been short-term, of less than two weeks, but many of these were continuous. The study of longest duration, 90 days, also used the lowest concentration of ethanol, 86 mg/m^3 (45 ppm); otherwise, experimental designs typically produced atmospheres of thousands of mg/m^3 (or ppm), frequently in order to develop ethanol dependence. Blood ethanol concentrations were often, but no always, determined. The great majority of BEC measurements were above 100 mg/dl.

The paucity of direct evidence regarding the possible effects of inhaled ethanol does not mean, however, that the possible consequences are unpredictable. In fact, the data strongly suggest that exposure of the general public to ethanol vapors coming from oxygenated gasoline is very unlikely to have any adverse consequences. While there is little, if any data, on the toxicity of ingested ethanol itself in humans, it is generally accepted that the vast literature on the effects of alcoholic beverages is highly relevant. Alcohol abuse is a significant medical and social problem, and is the impetus for most research into ethanol toxicology, both in humans and experimental animals. A consequence of this is that little experimental data address the levels of internal exposure that can be reasonably anticipated to result from using ethanol as an oxygenate. A second motivation for experimental work in ethanol is fetal alcohol syndrome (or fetal alcohol effects) which, in theory at least, could be caused by relatively brief maternal exposures to ethanol during pregnancy.

Since ethanol's important toxic effects require that the material first enter the bloodstream, one can evaluate inhalation exposures in terms of the blood alcohol concentrations they would produce. Prediction of BEC following exposure to ethanol vapors must consider several factors: (a) the concentration of ethanol in air, (b) the duration of exposure, (c) breathing rate, (d) absorption of ethanol across the lungs, and (e) the body's elimination rate of ethanol. Two of these factors are more or less constant in every situation. Experiments in humans have shown that from 55% to 60% of inhaled vapors are absorbed into the bloodstream (Kruhoffer, 1983; Lester and Greenberg, 1951). The rate of clearance of ethanol from the blood (V_{max}) is about 15 mg/dl/hr (Pohorecky and Brick, 1987) but may be as high as 23 mg/dl/hr (Holford, 1987); these rates correspond to elimination of 83 mg/kg/hr to 127 mg/kg/hr, or about 6 to 9 g of ethanol per hour for an adult. For comparison's sake, it should be noted that a single alcoholic drink contains about 12 g of ethanol (IARC, 1988).

As long as a person's intake of ethanol does not exceed V_{max}, blood alcohol levels will stay low. In Table 2 are shown the intake rates for ethanol inhaled under a variety of conditions, assuming absorption across the lungs of 55% and a standard body weight of 70 kg. In bold type are intakes above 83 mg/kg/hr, the lower estimate of alcohol clearance: exposure under these conditions could lead to an accumulation of ethanol in the blood and a rising BEC. Under the other conditions given, the body's ability to eliminate ethanol is not exceeded, and BEC levels would remain below toxic levels.

The calculations suggest that exposure to ethanol vapors that are irritating to the eyes and mucous membranes, while uncomfortable, would not cause a significant rise in BEC in persons at rest. As activity increases, ethanol intake increases, but vapor concentrations would need to exceed the occupational limit by a substantial margin in order to cause a rise in BEC. Some experimental work demonstrates that significant uptake of ethanol through the air is unusual, or difficult, as shown in Table 3. Moderate activity in the presence of irritating vapors is required.

Possible inhalation exposures to ethanol due to use in gasoline

Opportunities for inhalation exposure of the general public to ethanol used as a gasoline oxygenate include vapors inhaled while fueling vehicles and ambient air. The first sort of exposure would be relatively brief, no more than five minutes, perhaps, while the second could last for many hours. These scenarios are considered in more detail below.

Very limited investigations of personal exposures during refueling have so far failed to detect ethanol, where detection limits were 50 ppm or less (HEI, 1996). If refueling involved five-minute exposures at the occupational limit of 1,000 ppm, an adult might receive an ethanol dose of 0.13 g (about 2 mg/kg). Such an exposure might increase BEC by about 0.3 mg/dl, at most. Exposure to such a high level of ethanol is unlikely. The Health Effects Institute evaluated hypothetical exposures of 1 ppm for three minutes and 10 ppm for 15 minutes, and determined that incremental changes in BEC would be insignificant (HEI, 1996).

Data on ambient air concentrations of ethanol are few. The average ambient level in air in the city of Porto Alegre, Brazil, where 17% of vehicles run entirely on ethanol, is 12 ppb (0.023 mg/m^3) (Grosjean *et al*., 1998). The lowest concentration of ethanol tested for toxicity in animals was almost 4,000-times greater than this (86 mg/m^3, 45 ppm). A person might receive half a milligram of ethanol per day from ambient air containing 12 ppb of ethanol, a negligible dose.

Other health effects issues

Some of ethanol's known or suspected toxic effects have not been, or can not be, quantified in terms of BEC. Fetal alcohol syndrome (FAS), for example, is constellation of physical and mental deficiencies in children linked to maternal alcohol ingestion. Risk of FAS is a function of alcohol intake during pregnancy: the frequency of this syndrome is twice as great for children of heavy drinkers as for children of moderate or non-drinkers (Schardein, 1993). While it may be prudent to abstain from alcohol during pregnancy, a risk from daily consumption of less than 30 g of alcohol has not been proved (Schardein, 1993). Cancer of certain organs has been observed to occur at elevated rates in some groups of drinkers ,Äî the World Health Organization, for example, has linked alcohol consumption to cancers of the oral cavity, pharynx, esophagus, larynx, and liver (IARC, 1988). In almost all of the studies, risks were observed among alcoholics or were seen to increase with consumption.

Finally, if we look to human experience with alcohol consumption for information regarding toxic effects of ethanol, it is fair also to look at the evidence for possible health benefits. Numerous epidemiologic studies have observed that light-to-moderate drinkers of alcohol have lower mortality rates than either alcohol abstainers or heavy drinkers. Reduced mortality is due to decreased rates of fatal coronary heart disease and cardiovascular disease. To be sure, the picture is complicated, varying by sex, age, and disease risk factors, and competing causes of death. We are not suggesting that low-level exposures to ethanol due to its use as an oxygenate is desirable. At the least, however, the apparent beneficial effects of alcohol (or ethanol) for some cohorts should be recognized.

Conclusion

It is highly unlikely that exposure to airborne ethanol associated with gasoline use could produce toxic effects. The reasons for this are (a) the tiny doses that might be received, which might not be observable in light of endogenous levels of ethanol in blood, (b) the body's rapid elimination of ethanol, and (c) the relatively large doses of ethanol and high blood levels of ethanol associated with toxic effects in people. No data in the scientific literature support the hypothesis that chronic exposure to non-irritating levels of ethanol in air could cause significant elevation of BEC (unless exposed individuals are exercising at the time), or that a risk of cancer or birth defects would be created. A recent survey of the literature regarding the inhalation toxicity of ethanol by the Swedish Institute for Environmental Medicine reached similar conclusions, namely that "a high blood concentration of ethanol is needed for the development of adverse effects" and "ethanol at low air concentrations should not constitute a risk for the general population" (Andersson and Victorin, 1996).

Table 1: Ethanol Dose-Response Data

BEC (mg/dl)	Observation	Reference
0.02-0.15	Endogenous (*i.e.* natural) level	Jones, 1985; Lester, 1962
50	central nervous system stimulant; talkativeness; relaxation	Pohorecky and Brick, 1987
100	legal limit for automobile drivers in many states	
>100	central nervous system depressant; decreased sensory and motor function; decreased mental and cognitive ability	Pohorecky and Brick, 1987
110	no effect on heart function	Pohorecky and Brick, 1987
140	no effect on cerebral blood flow; effects occur above this level	Pohorecky and Brick, 1987
300	stupefaction	Pohorecky and Brick, 1987
400	possible lethal level	Pohorecky and Brick, 1987

Table 2: Intake Rate of Ethanol Under Various Exposure Conditions

Ventilation rate (l/min)	Intake rate of ethanol (mg/kg/hr) when the concentration in air is (mg/l)				
	1.9 (occupational standard)	5	10 (causes coughing and eye irritation; adaptation occurs)	20	30 (causes continuous lacrimation)
6 (rest)	5	14	28	57	**85**
25 (moderate	22	59	**118**	**236**	**354**

activity)					
40 (heavy activity)	36	**94**	**189**	**377**	**566**
50 (very heavy activity)	45	**118**	**236**	**471**	**707**

Table 3: Experimental studies of vapor uptake by humans

Ventilation rate (l/min)	Concentration of ethanol in air (mg/l)	Duration of exposure (hr)	BEC (mg/dl)	Symptoms	Reference
rest (approx. 6)	1.9	3	<0.2	none reported	Campbell and Wilson (1986)
15	15		steady at 7-8	vapors irritating but adaptation occurred; no intoxication	Lester and Greenberg (1951)
22	16	6	47 and rising	vapors irritating but adaptation occurred; no intoxication	Lester and Greenberg (1951)
rest (approx. 6)	maximum of 17 average approx. 9	2.5	<5	vapors irritating but adaptation occurred; no intoxication	Mason and Blackmore (1972)

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