

# Ethyl Glucuronide and Ethyl Sulfate Concentrations Following Inhalation of Ethanol Vapor

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## Introduction

Ethyl glucuronide (EtG) and ethyl sulfate (EtS) are minor nonoxidative direct biomarkers of ethanol ingestion.<sup>1,2</sup> The 2-5 day detection window of EtG and EtS is superior to direct ethanol measurements, which is approximately 1 hour per standard drink.<sup>1,2</sup> The sensitivity of EtG and EtS in urine for beverage ethanol consumption is greater than 90 percent and is therefore an extremely important assay for the early detection of relapse in alcohol abstinence programs.<sup>1,2</sup> Other indirect markers, such as CDT, GGT, MCV, EDAC, WBAA, and FAEE have sensitivities of less than 90 percent<sup>3</sup> and are therefore useless as a key indicator of relapse.

The controversy outlined in the Substance Abuse Treatment Advisory<sup>4</sup> raises the issue of the detection of EtG and EtS in urine as being too sensitive. To date, there is little if any published data on the correlation of unintentional ethanol exposure and the detection of EtG and EtS in urine.

One possible source of unintentional ethanol ingestion is the inhalation of ethanol vapor. Experiments in humans have shown that from 55% to 60% of inhaled vapors are absorbed into the bloodstream<sup>5,6</sup> The Odor Threshold of Ethanol is 0.1 mg/L.<sup>7</sup> OSHA requires the use of a respirator at an 8-hour weighted level of 1.9 mg/L.<sup>8</sup> Use of self-contained breathing apparatus with faceplate is required at a level of 6.2 mg/L.<sup>9</sup> Coughing and eye irritation is reported at 10 mg/L<sup>10</sup>. Using the OSHA Occupational Hazard Level of 1.9 mg/L and a ventilation rate for moderate activity (25 per minute), the intake of ethanol for a 70 kg person in an 8 hour day can be as high as 12.3 g or 1 standard drink and at the Odor Threshold the intake could be as high as 0.65g (0.05 standard drinks) .<sup>10</sup> Formation of metabolites following exposure to ethanol vapor depend on several factors: a) the concentration of ethanol in the air, b) the duration of exposure, c) breathing rate, d) absorption rate of ethanol across the lungs, and e) the body's elimination rate of ethanol.<sup>10</sup>

## Experimental

Inhalation of ethanol vapor was studied by adding approximately 50 mL of reagent grade ethanol to a 250 mL glass beaker. The beaker was swirled to wet the sides of the glass to promote vaporization. The beaker was held up to the nose and 1 deep respiration of vapor was performed. This procedure was carried out every five minutes for one hour. Urine specimens were captured at 15 minutes, 1 hour and approximately 14 hours (first void next morning). The specimens were analyzed at USDTL for creatinine and ethanol on an Olympus AU640 using standard protocols. The limit of detection for urine ethanol was 3 mg/dL. EtG and EtS determinations were performed at USDTL using standard protocols on an API 2000 LCMSMS. The limit of detection for EtG and EtS was 38.7 ng/mL and 7.2 ng/mL, respectively.

Both subjects reported that the fumes were noxious and irritating to the throat, lungs and eyes over time. Both subjects reported the odor to be sickening at approximately half way through the experiment. Because of the odor and irritation, both subjects refused a continuation study to determine if excessive conditions could generate positive EtG and EtS results.

## Study subjects

The two subjects that volunteered for this study are employees of USDTL. Subject A was a 64 kg 44 year old white female. Subject B was a 127 kg 41 year old white male. Both subjects are self reported social drinkers who abstained from social drinking during study segments.

## Results

Urine specimens were captured at 15 minutes, 1 hour and approximately 14 hours (first void next morning). The results for the urine specimens are outlined in Table 1. For purposes of comparison, the results were

Table 1. EtG and EtS results from Inhalation Study.

Subject	Time	Cre- atinine (mg/dL)	Ethanol (mg/dL)	EtG (ng/ mL)	EtS (ng/ mL)	Normal- ized EtG	Normal- ized EtS
A	0.25	36	<LOD	<LOD	<LOD	<LOD	<LOD
A	1.0	20	<LOD	<LOD	<LOD	<LOD	<LOD
A	14	156	<LOD	<LOD	<LOD	<LOD	<LOD
B	0.25	130	<LOD	<LOD	<LOD	<LOD	<LOD
B	1.0	195	<LOD	124	13	63	6
B	14	262	<LOD	<LOD	<LOD	<LOD	<LOD

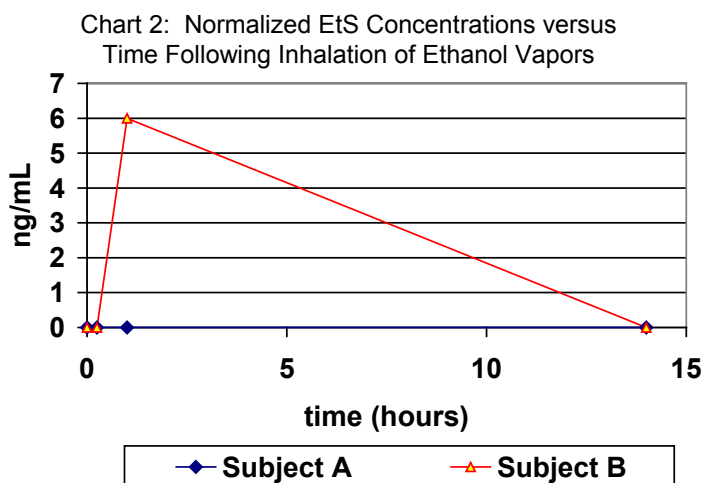
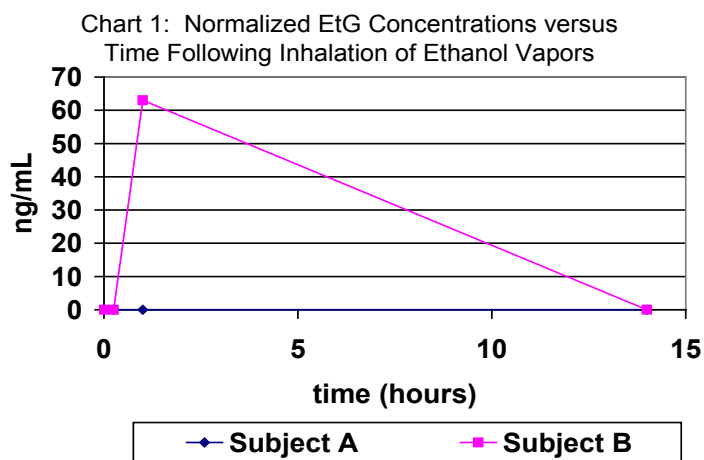
normalized to a creatinine level of 100 mg/dL in Table 1. Normalized EtG results are shown in Chart 1. Normalized EtS results are shown in Chart 2.

## Discussion

Ethyl glucuronide and ethyl sulfate are very sensitive direct biomarkers of ethanol intake, both intentional and unintentional. This study demonstrated that it is possible to generate detectable concentrations of EtG and EtS by direct inhalation of ethanol. One subject demonstrated no detectable levels of EtG or EtS. One subject demonstrated a detectable level at 124 ng/mL and 13 ng/mL, respectively. Considering the Odor Threshold of Ethanol, the results of this experiment, and the hundreds of negative results for hospital employees everyday (considering that most working areas of hospitals are above the odor threshold), it seems highly unlikely that exposure to ethanol in most workplaces will provide enough vapor to trigger a positive result. However, exposure to concentrations above the OSHA Occupational Hazard level may require further review.

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