Toxicokinetics of Ethyl Tertiary Butyl Ether in the Human Body

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(5)

Abstract: Ethyl Tertiary Butyl Ether (ETBE) is an additive in gasoline meant to reduce harmful emissions. ETBE has been introduced in the gasoline market as an oxygenate replacement for Methyl Tertiary Butyl Ether. But much testing needs to be done to make sure that ETBE exposure is not as harmful to humans as MTBE has shown to be. We used controlled exposure data from ten subjects, and created an exponential model to assess how ETBE behaves in the human body. We then incorporated new software to attempt to create a model that can represent an entire population.

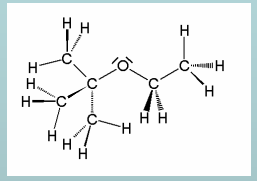


Figure 1. Structural Formula of ETBE (6)

Introduction:

-Oxygenated gasoline was required by the 1990 Clean Air Act Amendments to reduce air pollution.(1)

-ETBE is created by reacting ethanol with isobutene with heat over a catalyst. ETBE offers similar air quality benefits as MTBE or ethanol. (Fig. 1)

-In 1999 some states started to phase MTBE out and by 2000 the EPA recommended that it should be phased out completely. This was because it was showing up in drinking water sources. As more bans went into effect, it increased the need for ETBE and ETBE research.(1)

-Before there is widespread use and consequential exposure to ETBE. It is crucial to understand its toxicokinetics, or how ETBE absorbed, distributed, metabolized, and excreted in the human body.

Methods and Materials:

-Using new software called the System for Population Kinetics (SPK), a two-exponential model was defined.

-The ETBE breath concentration data from each of the ten subjects was entered into the model in the following format:

$$\textbf{Concentration} = A_1 e^{(-B1*TIME)} + A_2 e^{(-B2*TIME)}$$

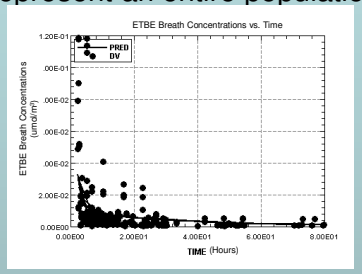
(Graph 1)

-The model accounted for the extent of physiological variability between the individuals through mixed effects modeling (including fixed and random parameter values)

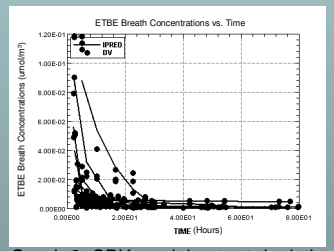
Results:

Labels	Fixed Parameter Value	Random Parameter Variability (%)	Random Measurement Variability (%)
A1	0.168	105	
A2	0.00991	155	
B1	0.844	280	
B2	0.0284	168	
σ			35.1

Table. Result Parameters



Graph 1. SPK model output depicting the average fit for all ten subjects.



Graph 2. SPK model output depicting individualized model fits.

Conclusion:

-Even with exposures of the same concentration of ETBE, breath concentration levels varied considerably.

-This can be seen in Graph #2 as well as in the Random Parameter Variability column in Table which has values ranging from 105-280%.

-Mixed Effects Modeling has allowed us to estimate:

- -Average decline in ETBE breath concentrations after exposure
- -Variability between subjects
- -Residual variability in measurements.

References:

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