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Analysis of toxic load calculations and fluctuation concentrations modeling for the assessment of atmospheric accidental release

Jean-Marc Lacome, Jean-Martin Vincent, Florence Zeman

INERIS, Parc Technologique ALATA, BP2, Verneuil en Halatte 60550, (France)

Corresponding author(s): Jean-Marc Lacome, Jean-Marc.Lacome@ineris.fr

Abstract:
Computing the effect zones around industrial facilities requires using modelling tools. For the specific case of accidental scenarios involving toxic cloud dispersion, it is necessary to make use of acute toxicity threshold values. Those thresholds can be given in terms of concentration or in terms of toxic load. The toxic load is commonly evaluated by extensions of the Haber's law that corresponds to an integration in time of concentration.
The improvements achieved in the atmospheric dispersion modelling now enable to predict the intermittency of the toxic cloud. However, such new approaches raise questions about the relevance of the toxic load evaluation, knowing that many parameters which characterize biological reality and the whole process of the dose-response should be taken into account. To achieve a deterministic model, it is necessary to pool research efforts between the communities of toxicologists and the atmospheric dispersion modellers.
This paper consists in confronting the level of knowledge of the fluctuation toxic cloud and biological parameters in the context of the deterministic modelling of consequences generated by an accidental toxic cloud.

Key words: *toxic load modelling, Haber's law, toxicokinetic model, fluctuation concentration*

INTRODUCTION

For the specific case of accidental scenarios involving toxic cloud dispersion, characterizing the effect zones around industrial facilities requires using modelling tools and make use of acute toxicity threshold values. A common practice consists in calculating toxic effects with the total inhaled dose. For some chemical, the time dependence of the exposure is important. For instance, inhaling a dose of ammonia over a short period could have much stronger effects on human health than inhaling the same dose over an extended period of time. The toxic load is commonly evaluated by extensions of the Haber's law, that corresponds to an integration in time of concentration, intended to account for this effect by using an exponent (example : $n > 2$ for ammonia) to the concentration inhaled. There are several extensions of the toxic load model that have been proposed to take into account that a toxic cloud is always intermittent in the real life. Indeed the cloud concentration is always varying due to many phenomena: atmospheric turbulence, momentum of the release, etc. The lack of toxic validation data enhances the difficulty to test the relevancy of toxic load models. Despite this lack of validation data many efforts are being provided to analyse theses toxic load models and to better assess its uses in function of chemical release scenario. Indeed, Urban et al. (2013) highlighted by predictions modelling of hazard area in case of chemical attack, that the choice of the toxic load model may be important in the case of realistic time – varying toxic exposure.
All these models are commonly used to calculate health effects with an inhaled total dose. This total dose is estimated by integrating the concentration evaluated by atmospheric dispersion modelling. A lot of scientific efforts have been produced to better assess fluctuations in the concentrations; however the inhaled total dose is estimated without taking into account physiological process that modify the accumulation process (Hilderman, 1999) of the total dose. In the same time there is a lack of knowledge to assess physiological response for very short time, i.e. less than 10 minutes. Therefore, difficulties exist in regulatory guidelines for very short time and for some chemical to determine load toxic thresholds.

The objective of this work is to estimate by a simple kinetic model, on the basis of concentration time series example, the effective arterial blood concentration that is expected to exceed a toxicological value. For each of this external concentration signal, the arterial blood concentration is calculated and compared to the safe target arterial blood concentration. This comparison allowed analysing effects of an external atmospheric concentration on the dynamic of the effective arterial blood concentration. This comparison gives also indications for the future on scientific research on atmospheric dispersion modelling to improve the assessment of fluctuations concentrations.

TOXIC LOAD MODELING AND CONCENTRATION FLUCTUATION IN TOXIC CLOUD: BRIEF REVIEW

Toxic load modeling

Concentration fluctuations in toxic gas dispersion are an important factor that is still difficult to assess in terms of atmospheric dispersion modeling and human toxic response. However most applied dispersion models ignore the fluctuations and predict only the mean concentration field. Sometimes this simplistic approach produces questionable input for most of the response model. Indeed, the damage is often related to some non-linear combination of atmospheric concentration, C, and duration of exposure, t such as $C^n t$, where $n > 1$. For a wide variety of industrial gases (see INERIS report), the exponent is higher than 1. Some years ago Griffiths and Megson (1984) and Mylne (1988) illustrated, with experimental data and over short periods, that a toxic amount 10 to 20 times higher can be reached with calculation based on instantaneous concentrations compared to a mean concentration.

Simple models are still currently used in the risk assessment to forecast mean concentration or relative "steady-state" concentration. As previously pointed by Nielsen et al. (2001) the use of a steady concentration raises difficult choice of model averaging time in order *to match the time-scale relevant for the risk analysis and enable model validation by field experiment*. Stochastic approach (Nielsen et al., 2001) or more deterministic sophisticated approach (Wilson, 1995), among relative simple models, have been proposed to address this issue. Moreover, scientific investigations are currently developed (Efthimiou et al., 20104; Bartzis et al., 2008) with CFD modelling approaches, such as RANS and LES, to predict the maximum dosage within a toxic cloud. However, few of these approaches are supported by regulatory guidelines or have been implemented in current software of the risk assessment. It could be explained by the complexity of the modelling approach but also due to the uncertainty related to the toxic threshold, above all for very short duration exposure (less than 10 minutes).

Experimental observations of a fluctuating toxic cloud

Since twenty years ago several gas tracer experiments have been carried in the free atmospheric boundary layer with full scale (Mylne and Mason, 1991; Mylne, 1992; Yee and Biltoft (2004)) or laboratory plume (Hilderman and Wilson, 2007). Experimental time series are generally described by using statistics parameters and their interrelationship, in particular the following one: the intermittency factor γ, the mean concentration C, fluctuation intensity $I = c'/C$, where c' is the standard deviation and C the mean concentration, and the fluctuation time scale T_c. The intermittency factor is defined by the proportion of time occupied by non-zero concentrations. The level of intermittency could directly influence the potential recovery process. Yee and Biltoft (2004) could show that, in urban environment, intensities of fluctuations are generally 2 to 5 times smaller than those measured on free environments. The fluctuation time scale, (the integral autocorrelation fluctuation of the turbulent concentration fluctuations), varies also depending on many parameters (wind speed, atmospheric turbulence, etc). The shorter the T_c, the faster the fluctuation process occurs. Experiments carried out by Mylne and Mason (Mylne and Mason, 1991; Mylne, 1992) showed that time integral scale could be greater in case of stable conditions relatively to neutral conditions. These results could have greater impacts in terms of damages. Indeed, the recovery process can decrease dramatically. At the opposite, peak with time scale concentration shorter than 1 s could be smooth out in the lungs.

MATERIAL AND METHOD

Material and toxic definitions

In order to illustrate intermittency impacts, we choose a Halocarbon-extinguish agent (2,2-dichloro-1,1,1-trifluoroethane or HCFC-123) which is a gaseous compound under normal aircraft operating conditions.

Halocarbons are relatively non toxic at recommended use concentrations (Tabscott and Speitel, 2002). However, even for brief exposures, the can induce cardiac arrhythmia at high concentrations in the bloodstream (Vinegar et al., 1998, 2000; Tabscott and Speitel, 2002; National Fire Protection Association, 2008) and can induce anesthetic effects for prolonged exposures as they accumulate in the organs and tissues.

No observable adverse effect level (NOAEL) and the lowest observable adverse effect level (LOAEL) are given in the Table 1 for 2,2-dichloro-1,1,1-trifluoroethane (HCFC-123). The NOAEL is the highest concentration (Lyon and Speitel, 2010) of the gaseous halocarbon in the air of the test environment at gaseous halocarbon in the air of the test environment at which none of the test animals exhibits any adverse physiological or toxicological effects. The LOAEL is the lowest concentration of the halocarbon in the test environment at which adverse physiological or toxicological effects are first detected. Consequently, the LOAEL represents a higher concentration of halocarbon in the air than the NOAEL. These limits are determined from gas concentration effect test data for beagle dogs exposed to various constant concentrations of halocarbon for 5 min combined with intravenous epinephrine at concentrations well above physiological levels.

Table 1. NOAEL and LOAEL concentrations, maximum safe 5-min human exposure concentrations, and target arterial concentration for HCFC-123

			Maximum safe 5-min human exposure concentration		Target arterial concentration, B_{safe} (mg/L)
Agent	NOAEL (%v/v)	LOAEL (%v/v)	(%v/v)	(mg/L)	(mg/L)
HCFC-123	1.0	2.0	1.28	78.9	69.9

Brief description of Kinetic model

Toxicokinetics (TK) is the quantitative study of factors that control the fate of chemicals within the body (Reddy et al., 2005). Toxicokinetic models provide a set of equations that simulate the time courses of chemicals and theirs metabolites in various tissues throughout the body.

The internal dose results from all toxicokinetic processes that occur in the body, divided into the processes of absorption, distribution, metabolism and elimination. Absorption is the uptake of chemical into the blood and lymph. Distribution can be defined as the transport of chemical in blood and accumulation in organs and tissues. Metabolism is the biotransformation into other products (metabolites) and may occur in various tissues. For some chemicals, the liver is the major metabolic organ, but a significant degree of metabolism may occur in other tissues as well. A chemical may be eliminated *via* exhalation, excretion through the kidney (urine) or liver (bile).

The relationships between tissue dose and exposure dose can be complex, especially in high-dose toxicity testing studies, with multiple, repeated daily dosing, or when metabolism or toxicity at routes of entry alter uptake processes for various routes of exposure (Reddy et al., 2005). Alterations in absorption kinetics (e.g., by changing dosage form or sometimes when giving the product with food) produce changes in the time profiles of the plasma concentration. Physiological and physico-chemical entities of the model structure include ventilation, blood flow (including cardiac output, arterial and venous blood flow) and biochemical expressions for metabolism, excretion and other processes that influence the toxicokinetic of the chemical.

The toxicokinetic model proposed by Lyons & Speitel (2010) predicts the blood concentration histories of human exposed to time-varying concentration of gaseous halocarbon fire-extinguishing agents such as HCFC-123. This model has been developed in the context of short term exposure (0-5 minutes). In the present work, this model has been used to predict the arterial concentration of HCFC-123 with different scenario of exposure. MCSim 5.0.0 (Bois and Maszle, 1997) has been used to implement the toxicokinetic model and to perform simulations.

In order to compare exposure concentrations to an internal level, a target arterial blood concentration at which cardiac sensitization occurs for a group of dogs exposed to the LOAEL (20 000 ppm exposure) for 5 minutes has been determined (Lyon & Speitel, 2010). The target arterial blood concentration was evaluated at 69.9 mg/L (see Table 1). This target arterial concentration has been shown to be the same for dogs and human (Vinegar et al., 1998) and provides the link for predicting safe 5 minutes human exposure concentration (Lyon & Speitel, 2010).

RESULTS AND DISCUSSION

Three time series of external concentrations were taken as input of the toxicokinetic model. These time series correspond to three scenarios of atmospheric concentration exposure with the same mean concentration $\overline{C}$ of 20 000 ppm exposure, corresponding to the LOAEL concentration, and the same toxic load, D(x), corresponding to a non-steady time varying concentration (equation (1)) :

$$D(x) = \int_0^T C(x,t)dt \qquad (1)$$

The three time series mainly differ from each other with the duration of the peak concentration.The first scenario depicts the condition of a 20 000 ppm steady exposure (LOAEL). Figure 1 show both the arterial blood concentration, calculated by the toxicokinetic model described previously, and the exposure concentration exposure. The results show as expected that arterial blood concentration calculated by the model is very close to the target arterial concentration (Bsafe). The peak of the arterial blood concentration exceeds to 5% of the target arterial concentration.

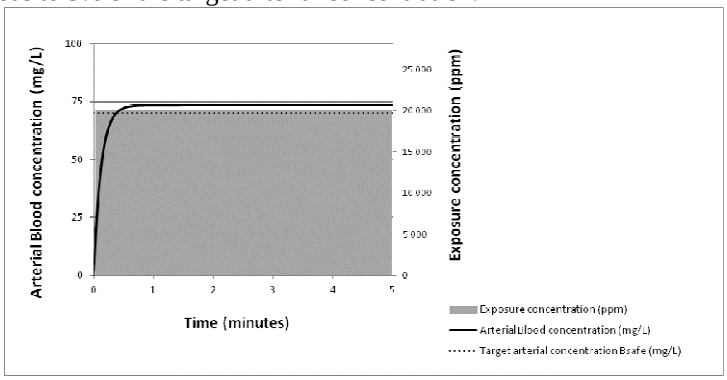

Figure 1: Simulation of arterial blood concentration using the toxicokinetic model for 5 minutes human exposure to constant HCFC-123 concentration of 20 000 ppm (LOAEL)

The second scenario simulates the conditions of time varying CFC-123 concentration with a sequence of alternatively repeated exposure to 10 000 ppm during 3 s with exposures to 30 000 ppm during 3 s. This short exposure is within the time range of a deep breath. By considering the value of 10 000 ppm as a background value (a zero value is usually considered in dispersion modelling), the intermittency, γ , is equal to 0.5. This is weak value that characterise very short time of peak exposure. The total intensity I = c'/C, where c' is the standard deviation, is equal to 0.5. Figure 2 shows both the arterial blood concentration, calculated by the toxicokinetic model described previously, and the exposure concentration exposure. In this scenario, the arterial blood concentration is fluctuating around the target arterial concentration. The peak of the arterial blood concentration exceeds to 20% of the target arterial concentration.

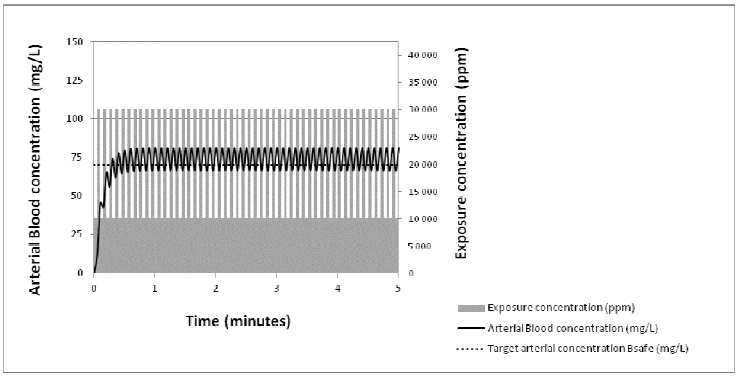

Figure 2: Simulation of arterial blood concentration using the toxicokinetic model for 5 minutes human exposure to time varying CFC-123 concentration of exposure (exposure to 10 000 ppm during 3s then 30 000 ppm during 3s)

The third scenario reproduces the conditions of time varying CFC-123 concentration with a sequence of alternatively repeated exposure to 10 000 ppm during 30 s with exposures to 30 000 ppm during 30 s. The intermittency and the intensity are equal to the ones of the previous scenario. Figure 3 shows clearly that the calculated arterial blood concentration exceeds the target arterial concentration. It should be noticed, that this time the peak of the arterial blood concentration is up to 50% of the target arterial concentration.

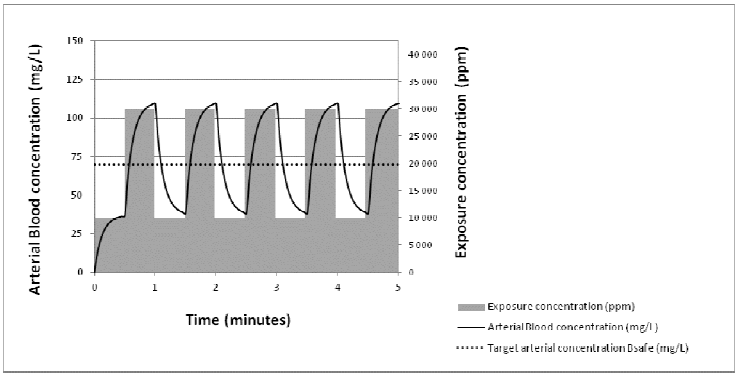

Figure 3: Simulation of arterial blood concentration using the toxicokinetic model for 5 minutes human exposure to time varying CFC-123 concentration (exposure to 10 000 ppm during 30s then 30 000 ppm during 30 s)

Although the mean external concentration and external dose are equivalent for the three scenarios, we observed that the peaks of arterial blood concentration exceed to 5%, 20% and 50% the target arterial concentration respectively. This result can be explained by the influence of the peak exposure time which differs according the three scenarios.

These preliminary and academic results emphasize the influence of the peak exposure time on the arterial blood concentration for short total exposure times and the need to correctly asses it by atmospheric modelling.

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