QSARs for the Fiftieth Anniversary of the RD50

Yves Alarie, Ph.D., Professor Emeritus, Graduate School of Public Health, University of Pittsburgh

ABSTRACT

In 1966, Alarie, Y. (Arch. Environ. Health 13: 433-449) published a bioassay to evaluate the potency of airborne chemicals (vapors and aerosols) as sensory irritants. The potency was expressed as the exposure concentration resulting in a characteristic decrease in respiratory rate by 50% (RD50) in mice. The bioassay became widely used and RD50s were obtained for 83 industrial chemicals (Alarie, Y. 1973 CRC Crit. Rev. Toxicol. 2: 250-263). A large database (244) of RD50s and Threshold Limit Values (TLVs) was available as well as LOAELs and NOAELs. Schaper et al. (1993) used the same VOCs database. From this database, RD50s were also obtained for 83 reactive (rVOCs) and 99 nonreactive (nrVOCs) chemicals. These chemicals were evaluated using both RD50s and TLVs. Excellent QSARs were obtained for rVOCs and reactive (rVOCs) but not for nonreactive (nrVOCs). For rVOCs, their potency was explained by separating them on the basis of specific reactivity mechanisms. Recently, Gupta, S. et al. (Ecotoxicology 2015, 24:873-886) used the same VOCs database. First they were able to differentiate the rVOCs from the nrVOCs and then predicted the RD50s for both groups. This was achieved on the basis of decision tree classification followed by regression methods using selected molecular descriptors. Thus the use of QSARs capable of predicting RD50s, LOAELs or TLVs as regulatory purposes, for r or nrVOCs is within reach. Not so yet for solids or for liquids of very low vapor pressure, encountered in the aerosol state. The following will be presented and discussed and will be available at www.pitt.edu/~rd50 for investigators to use to further improve predictive models using various approaches.

REFERENCES

1. Normal Airflow (Vdot) and tidal volume (VT) in mice. Arch. Toxicol. 68: 490-499.
2. Pulmonary irritation (P)

MOUSE BIOASSAY: HISTORY

Legend for Figures

1. (A) Inhalation bioassay in mice (Alarie, 1966)
2. (B) Breathing patterns in mice (normal breathing and braking)
3. (C) Concentration-response relationship using (a) CBMN and DACA, as obtained in mice

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