Designation: E1242 – 23

Standard Practice for Using Octanol-Water Partition Coefficient to Estimate Median Lethal Concentrations for Fish Due to Narcosis[1]

This standard is issued under the fixed designation E1242; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This practice covers a procedure for estimating the fathead minnow (*Pimephales promelas*) 96-h LC50 of nonreactive (that is, covalently bonded without unsaturated residues) and nonelectrolytic (that is, require vigorous reagents to facilitate substitution, addition, replacement reactions and are non-ionic, non-dissociating in aqueous solutions) organic chemicals acting solely by narcosis, also referred to as Meyer-Overton toxicity relationship.[2]

1.2 This procedure is accurate for organic chemicals that are toxic due to narcosis and are non-reactive and non-electrolytic. Examples of appropriate chemicals are: alcohols, ketones, ethers, simple halogenated aliphatics, aromatics, and aliphatic substituted aromatics. It is not appropriate for chemicals whose structures include a potential toxiphore (that structural component of a chemical molecule that has been identified to show mammalian toxicity, for example CN is known to be reponsible for inactivation of enzymes, NO_2 for decoupling of oxidative phosphorylation, both leading to mammalian toxicity). Examples of chemicals inappropriate for this practice are: carbamates, organophosphates, phenols, beta-gamma unsaturated alcohols, electrophiles, and quaternary ammonium salts.

1.3 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[3]

E729 Guide for Conducting Acute Toxicity Tests on Test Materials with Fishes, Macroinvertebrates, and Amphibians

E943 Terminology Relating to Biological Effects and Environmental Fate (Withdrawn 2023)[4]

E1023 Guide for Assessing the Hazard of a Material to Aquatic Organisms and Their Uses

E1147 Test Method for Partition Coefficient (N-Octanol/Water) Estimation by Liquid Chromatography (Withdrawn 2013)[4]

3. Terminology

3.1 *Definitions:*

3.1.1 *acute toxicity*—where an adverse effect such as mortality is measured after organisms exposed to a compound for a relatively short period, usually not constituting a substantial portion of their life span.

3.1.2 *narcosis, n*—a reversible state of stupor, unconsciousness, or arrested activity produced by the influence of chemicals on critical sites within membranes or by disrupting the normal functioning of certain proteins by means of nonspecific binding of organic chemical(s) to hydrophobic sites. Death results if exposure is not terminated after a length of time which varies with concentration.

3.1.3 *octanol-water partition coefficient (K_{ow}), n*—referred to as *P* in some literature.

3.1.4 *toxiphore, n*—a chemical structure substituent group that when present gives rise to an adverse effect in exposed organisms.

[1] This practice is under the jurisdiction of ASTM Committee E50 on Environmental Assessment, Risk Management and Corrective Action and is the direct responsibility of Subcommittee E50.47 on Biological Effects and Environmental Fate.

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[2] Lipnick, Robert L., "Validation and Extension of Fish Toxicity QSARs and Interspecies Comparisons for Certain Classes of Organic Chemicals," *QSAR in Toxicology and Xenobiochemistry*, Elsevier, 1985.

[3] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

[4] The last approved version of this historical standard is referenced on www.astm.org.

4. Summary of Practice

4.1 The hydrophobicity of a non-reactive and non-electrolytic organic chemical as quantified by log of the octanol-water partition coefficient is substituted into an experimentally derived equation and an approximate 96-h log LC50 for fathead minnow is calculated. This value is a maximum value. The actual LC50 could be lower, but should not be higher.

4.2 For definitions of other terms used in this practice, refer to Guide E729, Terminology E943, and Guide E1023.

5. Significance and Use

5.1 This procedure can be used to limit the need for screening tests prior to performing a test for estimating the LC50 of a non-reactive and non-electrolytic chemical to the fathead minnow. By eliminating the screening test, fewer fish need be tested. The time used for preparing and performing the screening test can also be saved. The value obtained in this procedure can be used as the preliminary estimate of the LC50 in a full-scale test.

5.2 Estimates can be used to set testing priority of groups of non-reactive and non-electrolytic chemicals.

5.3 If the estimated value is more than 0.3 times the experimental value, the mechanism of action is probably narcosis. If less, the effect concentration is considered to reflect a different mechanism of action.

5.4 This practice estimates a maximum LC50, that is, non-reactive and non-electrolytic chemicals are at least as toxic as the practice predicts, but may have a lower LC50 if acting by a more specific mechanism. Data on a chemical indicating a lower toxicity than predicted should be considered suspect or an artifact because of limited solubility of the test material.

6. Procedure

6.1 Review other toxicity data on the test material to see if the test material is likely to cause acute toxicity by a mechanism other than narcosis. Also, review the structure of the test material for toxic substructures. If there are no toxiphores present or other data which indicate the non-reactive and non-electrolytic chemical will be acutely toxic by a mechanism other than simple narcosis, this procedure will provide a maximum 96-h LC50 estimate or hypothetical narcosis 96-h LC50.

6.2 Obtain the octanol-water partition coefficient (K_{ow}), by measurement (see Test Method E1147), from a literature source or by estimation based on structure.[5] Since the K_{ow} value is critical to calculating the LC50, it is important to obtain a measured value rather than depending completely on literature or estimation based on structure.

6.3 Derive the relationship between the LC50 and K_{ow} in the form:

$$\text{Log LC50} = a\log K_{ow} + b\log(c\,K_{ow} + 1) - d \quad (1)$$

using the bilinear model of Kubinyi.[6,7] Calculate the Coefficient of Determination (R^2).

6.4 Using this relationship, calculate an estimated LC50 for additional non-reactive and non-electrolytic chemicals for which the K_{ow} is known or estimated.

6.5 Compare the calculated 96-h LC50 with solubility to be sure it is equal to or less than the solubility limit. If the estimated LC50 is greater than the solubility, the chemical is probably not lethal at the highest possible dissolved concentration in water.

7. Report

7.1 Report the following information:

7.1.1 The coefficients derived using the relationship in 6.3 and the coefficient of determination,

7.1.2 The estimated 96-h LC50 for a non-reactive and non-electrolytic chemical of interest based on the derived relationship,

7.1.3 Sources of data for LC50 and K_{ow} from which the relationship was defined,

7.1.4 Source of the K_{ow} for a non-reactive and non-electrolytic chemical of interest,

7.1.5 Name and contact information of the persons making each derivation of the LC50 K_{ow} relationship and estimates, and

7.1.6 Date of the estimates.

[5] Great Lakes Water Quality Initiative Technical Support Document for the Procedure to Determine Bioaccumulation Factors Appendix A, Procedure for Deriving Recommended Values for Log K_{ow}, EPA-820-B-95-005, 1995.

[6] Kubinyi, H., "Non-Linear Dependence of Biological Activity on Hydrophobic Character: The Bilinear Model," *Farmaco (Pavia) Ed. Sci.*, Vol 34, pp. 248–276.

[7] Veith, G. D., Call, D. J., and Brooke, L. T., "Structure-Toxicity Relationships for the Fathead Minnow, *Pimephales promelas* : Narcotic Industrial Chemicals," *Canadian Journal of Fisheries and Aquatic Sciences*, Vol 40, 1983, pp. 743–748.