

“ LD₅₀ ” [LETHAL DOSE 50%]

This Note is designed to provide guidance to RSC members, though it may also be useful to others with a particular interest in the subject. It is an update of the original version which was issued in 1996.

The LD₅₀ test and its variants were often undertaken as a result of legislative requirements. These tests are now considered obsolete and nowadays they would rarely if ever be performed in the United Kingdom and many other countries. Internationally accepted alternative tests have been developed. These use fewer animals and “absence of evident toxicity”, rather than death, as their criterion. They have been accepted by most regulators as valid alternatives to LD₅₀ testing.

Nonetheless LD₅₀ values are still quoted and enquiries received by the Royal Society of Chemistry suggest that there is still a need for information about their meaning. This Note aims to provide basic information about LD₅₀ but does not pretend to be a full or definitive explanation. Readers are urged to obtain more detailed information if this is required. Also this paper does not address the complex ethical arguments surrounding the use of animal experiments to obtain LD₅₀ and related data.

WHAT IS AN LD₅₀?

“LD₅₀” is an abbreviation for “Lethal Dose 50%.” It is sometimes also referred to as the “Median Lethal Dose”. Although the LD₅₀ is no longer the only measure available for assessing the acute toxicity of single doses of a substance, for historical reasons it is probably still the most commonly cited measure.

The LD₅₀ for a particular substance is essentially the amount that can be expected to cause death in half (ie 50%) of a group of some particular animal species, usually rats or mice, when entering the animal's body by a particular route. For example if the substance is swallowed the figure is an ‘oral LD₅₀’ whereas if its absorbed through the skin it's a ‘dermal LD₅₀’. LD₅₀ figures are derived by mathematical calculation from the results of tests on animals and hence should not be regarded as biologically precise values. In general the amounts of a substance required to kill animals from different species are approximately related to the animals' body weights. Therefore LD₅₀ figures are usually reported in units of milligrams of the substance per kilogram body weight for the animal species concerned.

The LC_{(t)50} (lethal concentration 50% for exposure time t) is a similar and widely used measure for acute toxicity by inhalation. The LC_{(t)50} is essentially the concentration of a substance that can be expected to cause death in half [ie 50%] of a group of some particular species

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when entering the body over the specified period of time. “LC_{(t)50}” figures are usually reported as milligrams of the substance per cubic metre (or litre) of the atmosphere to which the animal is exposed for the specified time [t]. Generally, no account is taken of body weight when comparing values for different species.

Conventionally, the median lethal dose (MLD) is quoted as an LD₅₀ when the exposure is by swallowing, skin contact or injection and as an LC_{(t)50} when exposure is by breathing it in. When quoting an LD₅₀ the information must include the substance, the route of entry and the animal species. For example sodium cyanide has an oral LD₅₀ of 15 mg/kg in rats. The LC_{(t)50} of a substance should state the duration [t] and species.

From the above it will be clear that the smaller the LD₅₀ or LC_{(t)50} figure the less the amount of the substance needed to cause death.

In environmental toxicology the concentration of a substance which may be lethal to wildlife may also be expressed as LC_{(t)50} figures where the concentration [c] refers to the concentration in the relevant environmental medium. Perhaps the most common such use is LC_{(t)50} in water to indicate aquatic concentrations lethal to fish species. However LC_{(t)50} values can also be given for a substance in soil or other materials.

WHAT USE IS AN LD₅₀ FIGURE?

Most users of a substance will need to know its toxicity to humans. It requires expert judgement to assess the relevance to humans of toxicity data derived from animals, including LD₅₀ figures. Under European law the supplier of a chemical substance must assign it to a defined toxic hazard category using criteria set out in the legislation. The supplier may use LD₅₀ figures, among other data, when deciding how to categorise the substance. Alternatively they can use a categorisation system based on a lack of “evident toxicity”.

Information from either procedure may be used to classify the acute lethal hazard of a substance as set out in the regulatory requirements (eg “very toxic if swallowed”). LD₅₀ and LC_{(t)50} values themselves give no information about other, non-lethal, effects of the substance, nor about cumulative, chronic, reproductive or irritant effects.

The law requires that the supplier of a substance must classify and label it to show the hazard categories to which it belongs and provide a material safety data sheet (MSDS) that gives, amongst other things, the hazard categories that apply to the substance. The relevant MSDSs will provide much, but not all, of the information that must be taken into account when making a COSHH assessment and deciding on appropriate control measures for use in the workplace. [Information will also be needed on the circumstances of use and hence the likely exposures.] The MSDS also provides information needed when classifying wastes as “special wastes”. Information on the LC_{(t)50} values can also be used when preparing safety reports for toxic major accident hazards.

Some people have doubts about the ethics of using animals to obtain toxicity data. The complex ethical, legal and scientific issues involved are beyond the scope of this paper. However, toxicologists have developed new procedures that reduce the numbers of animals used for acute toxicity testing and they continue to seek alternative, non-animal based procedures for assessing acute toxicity.

FURTHER READING

- Hayes, A., 'Principles and Methods of Toxicology', Taylor and Francis, 4th Ed, 2001, Chapter 18
- Gad, S., 'Acute Toxicology Testing', The Telford Press, 1988, Chapter 7
- The British Toxicology Society, 'A New Approach to Classification of Substances and Preparations on the Basis of their Acute Toxicology', 1984, Human Toxicol., Vol 3, 85-92

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