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Water as a Standard Substance of a Logarithmic Poison Scale

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Abstract

The lethal dose LD_{50} represents the most important experimental value for acute toxicity. The simple logarithmic calculation of $-\log_{10} LD_{50}$ = value leads to the possible poison power pLD. As with the pH or pK value, respectively, for acid or the scale of earthquake intensities the logarithm helps making large differences of orders of magnitude easier to understand since they are more comparable. The higher the pLD value, the higher is the power of poison. An increase of the pLD value by 1 stands for a tenfold increase in toxicity. The lethal acute dose for water, one of the most important and at the same time non-toxic substances of all, is about one tenth of the body weight. This leads to a possible pLD value for water of 1, an ideal starting value for a logarithmic poison scale.

Keywords

LD_{50}, Lethal Dose, Toxicity, Water, Glyphosate, Poison Scale

1. Introduction

Water is essential for life. The idea that water could be poisonous seems absurd at first glance. However, there have been repeated attempts to determine the lethal dose of water. In 1916, for example, J. G. Priestley drank three liters of water within a short period of time, but could not detect any impairment [1]. In 1926, dermatologists Amberg and Austin consumed the same amount to study the effect of water intake on skin elasticity and experienced violent muscle twitching. The planned study of the skin was no longer possible [2]. In 1956, there was a study in which even an amount of 90 g/kg body weight in rats resulted in a miserable condition but not death [3]. Transferred to a human weighing about 70 kg, this would be the rapid ingestion of about 6 L of water.

In fact, this amount seems to be a potentially lethal dose, because there are

repeated cases where the rapid and excessive consumption of this amount of water has led to significant health problems and even death.

Within one hour a healthy kidney can excrete about 800 to 1000 ml of water. When more than one liter is consumed, water reaches regions of the body with higher salt concentrations. Not the too much water, but the decreasing amount of sodium ions due to dilution with water becomes the crucial problem. Too much water means a decrease in sodium ion concentration and thus osmolarity in the extracellular space, causing cells to swell. This happens especially in brain cells, so CNS disorders such as headache and confusion are the first symptoms of hyponatremia. This is followed by muscle tremors and seizures. A decrease in the normal plasma sodium level from 144 mmol/l to below 120 mmol is considered life-threatening [4]. Since the deficiency of sodium ions is the reason for water intoxication, the obvious therapy remains the supply of sodium chloride.

Underestimated is the oversupply of water also in marathon events. In 2002, a study at the Boston Marathon found 35% of participants had increased weight after the race [5].

Cases of water intoxication found in the literature include the following:

- In 2003 the British actor Anthony Andrews survived a case of water intoxication. He was performing as Henry Higgins in a revival of the musical My Fair Lady at the time, and consumed up to eight litres of water a day. He was unconscious and in intensive care for three days [6].
- In January 2007 Jennifer Strange died after drinking nearly 2 gallons (7.6 liters) of water in an attempt to win a Computer game. A radio station's morning show held an on-air contest entitled "Hold Your Wee for a Wii," in which contestants were asked to drink as much water as they could without urinating. The DJs were made aware of the dangers but did not inform the contestants [7].
- In March 2020 Zachary Sabin, an 11-year-old child, died after being forced to drink almost three liters of water in just four hours by his parents. They thought his urine was too dark, so they made him drink water until he threw up [8].

The examples cited suggest a potentially life-threatening dose of 6 to 7 L of water, or 90 g/kg body weight, is realistic.

2. Results

Considering the fact that the dose makes the poison a reference value has been found in order to demonstrate the toxicity of a substance. A very frequently used factor is the lethal dose LD_{50}. LD_{50} signifies the mean lethal concentration *i.e.* the quantity that leads to death of 50% of all laboratory animals mostly rats. In order to provide comparability with human beings, the value is indicated as quantity of poison (mostly by oral intake) per kilogram body weight. The concept of the lethal dose LD was introduced by J. W. Trevan in 1927 [9]. The LD_{50} values exhibit an extremely broad range. While the LD_{50} value of water is over 90 g/kg

body weight [3], the diphtheria toxin has an LD_{50} of 300 ng/kg. The probably most toxic substance in the world, the botulinum toxin, even reaches the value of 30 pg/kg with, however i.v. [10]. It is thus a matter of values in ratios of more than one in a trillion.

So, it would make sense to simplify the previous representation in order to achieve a better understanding and a rapid comprehension of the acute toxic potentials.

There are many physical figures with tremendous differences in size where the logarithmic representation prevailed. Here we must recall the important pH value which specifies the concentration of protons in aqueous solutions [11], the pK_a value which is characteristic of the acidity of Brønsted acids, or the renowned Richter magnitude scale which assigns a magnitude number to quantify the violence of an earthquake [12]. Moreover, with the consideration of LD_{50} values the indication in pure SI units kg would be appropriate. In doing so, the units in the LD_{50} values are already reduced. Following the application of the common logarithm and for the sake of simplicity, as already done with the calculation of pH values, there is a change of sign. With this, only positive values are obtained [13].

As the small "p" in the pH value is derived from the Latin word pondus (= weight, load or force) [14] LD_{50} values become pLD values. The indication of more than one place after the decimal point would suggest a non-existing accuracy in the toxicological practice. Many LD_{50} values given in the literature pretend to be accurate with several digits, which is not the case. This is a further argument to use pLD values with only a few digits. As a name for this new value pLD I propose *poison power*.

$$-\log_{10} \mathrm{LD}_{50}\left(\frac{\mathrm{kg}}{\mathrm{kg}}\text{body weight}\right) = \mathrm{pLD}$$

It is useful to use standardized LD_{50} values for oral intake in rats to classifying pLD values because these LD_{50} values are most commonly used for the lethal dose. The possibly least non-toxic substance is normal water. As mentioned the LD_{50} value for water is over 90,000 mg/kg, *i.e.* 0.09 kg/kg [3]. The common logarithm of 0.09 is therefore −1.045. After change of sign the result obtained is 1. Thus, water has a pLD value of 1.

$$-\log_{10} 0.09 = 1 \quad \mathrm{pLD}_{\mathrm{water}} = 1$$

An augmentation of the pLD value by 1 results in a tenfold increase in toxicity.

Table 1 presents a small selection of substances, their corresponding LD_{50} values and the derived pLD values.

The resulting poison scale provides a quickly to understand overview or the acute toxicities which are easy to compare.

The corresponding poison scale which can be obtained from the pLD values, is unlimited. The pLD value is a simplification compared to the LD_{50} value. At the same time there is no loss in quantitative precision. Every compound is connected to a pLD value and every substance can be more or less toxic.

Table 1. Poison power pLD = $-\log_{10}$ LD_{50} (in kg/kg body weight) for rats, oral intake.

Substance [Ref.]	LD_{50}		
	Descent	mg/kg	pLD
2,3,7,8-Tetrachlorodibenzodioxin [15]	Industrial waste	0.02	7.7
Parathion [16]	E 605	2	5.7
Potassium cyanide [17]	Gold leaching	5	5.3
Citrinin [18]	Mushroom poison	134	3.9
Ephedrine [19]	Cough syrup	600	3.2
Sodium chloride [20]	Table salt	3,000	2.5
Glyphosate [21]	Herbicide	4,873	2.3
Ethanol [22]	Alcohol	7,060	2.2
Sucrose [23]	Household sugar	32,500	1.5
Water [3]	Tap water	More than 90,000	1

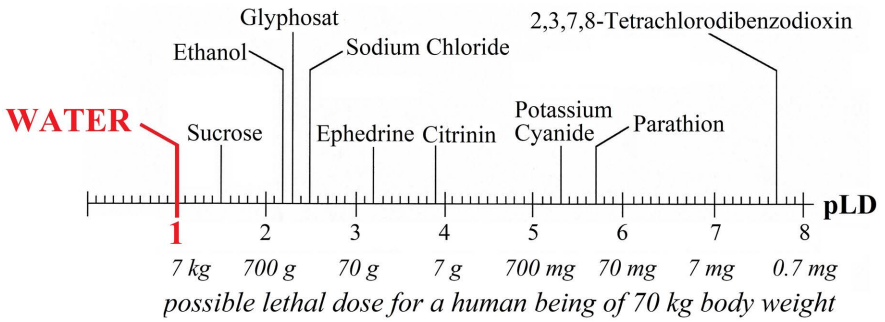

Figure 1. Poison scale: pLD value of different compounds. Water has a standard value of 1.

A compound with a pLD of 6 must therefore be taken in a body with a weight proportion of one to one million, as the negative logarithm of one million is 6. Mercury (II) chloride, the classical sublimate, has exhibits a value of 1 mg/kg [24] and thus a pLD value of 6.

The scale in Figure 1 obviously shows that the acute toxicity of the recently very controversially discussed herbicide glyphosate is situated between ethanol and sodium chloride.

Toxicologists repeatedly use the LD_{50} test as the first step in assessing the toxicity of a substance. However, this value is controversial among biologists and ethicists. The LD_{50} test does not comply with the principle of minimizing or completely avoiding the use of animals in toxicity tests. In 2002, the Organization for Economic Cooperation and Development (OECD) deleted the LD_{50} test as a requirement for testing new chemicals. The OECD replaced the classical LD_{50} test with three alternative tests: the fixed dose procedure (FDP), the acute toxic class method (ATC), and the up and down procedure (UDP), [25]. Furthermore, the LD_{50} values determined to date also differ considerably in some cases for different test animals. For example, an LD_{50} value of 0.18 mg/kg was

found for oral intake of the cardiac glycoside in cats, while in rats the value was 56 mg/kg. [26]. It has long been known that LD_{50} values are not regarded as biological constants [27]. The transferability of medical effects determined in animal experiments to humans also has its limits: Humans are definitely no 70-kg mice [28]. However, it is to be expected that the rapid development of artificial intelligence will considerably simplify the prediction of the toxicity of new substances in the future. For the development of new drugs, it is essential to have reliable methods in order to avoid costly failures. It is estimated that over 30% of potential drug candidates are discarded owing to toxicity [29].

3. Conclusion

It is remarkable that the most non-toxic substance of all, water, has an easy-to-remember starting point for a logarithmic toxicity scale with the value one. It is useful to use standardized LD_{50} values for oral intake in rats to classifying pLD values because these values are most commonly used for the lethal dose. The proposed model naturally has its limits in the extent to which measured or predicted LD_{50} values can be precisely determined at all and only concern acute toxicity. A particular challenge would be to quantify the long-term toxicological potential of compounds, especially environmentally harmful hazardous substances such as halogenated hydrocarbons or polycyclic aromatics, and to make them more comparable. The new possibilities of artificial intelligence could be helpful in the future.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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