v. 3, n. 4, 2023

Journal of
Agricultural
Sciences
Research

THE LD50 IS AN INSUFFICIENT FOUNDATION FOR THE SAFE HANDLING OF INSECTICIDES

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Abstract: The toxicity of insecticides is expressed by the lethal dose 50 (LD50) which indicates the quantity necessary to kill 50% of the tested population. Frequently, there is a misinterpretation of this value when it is assumed that, for a pesticide to cause death, the person must consume an amount close to the LD50, when insecticides actually cause death at doses below the LD50. The objective of this work was to present a numerical exercise to show that the LD50 does not indicate that intakes below the LD50 are also lethal. For this, a numerical exercise was performed based on the LD50 of dimethoate (250 mg/kg). First, a regression equation y=a+bx was constructed based on the probit=5 value corresponding to the LD50. The ordinate to the origin ("a") was solved using a hypothetical value of b=1.0 In such a way that the equation was: 5=a+1(2.398=log of 250=). So, "a" was solved like this: a=5-1(2.398)=2.602. Therefore, the equation for an LD50 was: 5=2.602+1(2.398). Later, to calculate the LD10 and the LD1, the probit value=5 was replaced by the probit value (value of "y") corresponding to the LD10 (=2.67) and the LD1 (=3.72), based on Finney (1964). Solving for "x", for obtaining the LD10 value was = 13.12, mg/kg while the "x" value for the LD1 was = 1.17 mg/kg. This numerical exercise showed that dimethoate doses were lower than the LD50 (250.0 mg/kg). The LD10 (13.12 mg/kg) and the LD1 (1.17 mg/kg) can kill 10 and 1%, respectively, of the population that consumes such quantities.
Keywords: Toxicity, Health risk, Probit analysis.

INTRODUCTION

The lethal dose 50 (LD50) is a universally accepted indicator to express the toxicity of registered insecticides. This indicator expresses the amount of active ingredient, in mg/kg of live weight, necessary to kill 50% of the population under test (Castro De La Mata, 1996). Frequently, there is a misinterpretation of this value when it is assumed that, for a pesticide to cause death, the person must consume an amount close to the LD50, when insecticides actually cause death at doses below the LD50. Furthermore, it must be kept in mind that the LD50 is an indicator applicable to populations rather than to an individual effect.

The Spearman Karber methods and the transformation of mortality percentages to Probit values are accepted by the World Health Organization (WHO) in the evaluation of acute toxicity. Therefore, they have been established as routine procedures in laboratories dedicated to toxicological studies in different countries (Gene and Robles 1987 and Castro De La Mata, 1996).

According to ENTOLUX (2018), the WHO has classified toxic active ingredients into five categories according to their LD50: extremely dangerous (up to 20 mg/Kg in liquids and up to 5 mg/Kg in solids), very dangerous (from 20 to 200 mg/Kg in liquids and from 5 to 50 mg/Kg in solids), moderately dangerous (from 200 to 2000 mg/Kg in liquids and from 50 to 500 mg/Kg in solids) little dangerous (from 2000 to 3000 mg/Kg in liquids and from 500 to 2000 mg/Kg in solids) and those that normally do not offer danger (More than 3000 mg/Kg in liquids and more than 2000 mg/Kg in solids).

This classification makes it possible to judge the risk of poisoning to humans and domestic animals that each active ingredient on the market represents. In addition to the lethal effects of toxic substances on the market, other significant damage to human health are not considered as classification criteria. However, severe damage has been recognized on the central nervous system, the peripheral nervous system and the sense organs. Consistent with this vision, the classification proposed by Vela, Laborda and García (2003) contains four levels of genotoxicity, such as: mutagenicity, chromosomal aberrations, carcinogenicity [Klaassen (2008); Environmental Protection Agency (2005) and Meco, Bonifati, Vanacore and Fabrizio (1994)]. Despite the fact that the effects described above are known and documented, in daily chemical control, the level of toxicity is still based only on the LD50 (Silva 2001).

Unfortunately, the LD50 value is often misinterpreted. It is generally assumed that consumers of contaminated food would be at risk of death only when they ingest an amount of the poison close to its LD50 value. Considering this unfortunate conception of the LD50, the objective of this work is to show, numerically, that insecticides can cause deaths, even at doses much lower than their respective LD50.

MATERIALS AND METHODS

This exercise is based on Probit analysis, thanks to which the LD50 value is obtained. The mortality percentages of a bioassay are analyzed to solve the regression equation: y=a+bx where:

y=5 which is the probit value for the LD50 (Finney (1964).

a=Ordered to the origin

b= Slope of the regression line

x= Log dose. For the LD50 of dimethoate it is 250 mg/kg, whose log= 2.398.

b=1 Hypothetical value, since it does not exist in the data sheet.

The technical sheet of the insecticides does not contain the regression equation from which the LD50 value was calculated. Therefore, the value of "b" (slope of the regression line) is unknown despite being essential to solve the regression equation. Consequently, for an exercise for this purpose, a hypothetical value can be assigned. In this exercise it was b=1. Of course, changes in the value assigned to "b" alter the result of the resulting DL. Unfortunately, there is no other way around this omission from the data sheet.

RESULTS AND DISCUSSION

With the data reported in methodology, the regression equation (y= a+bx) for the LD50 of dimethoate= 250 mg/kg was resolved as follows:

5=a+1(2.398=250 log).

In this equation, the value of "a" was solved this way: a= 5-1(2.398)= 2.602.

Once the members of the equation for the LD50 were substituted, it was resolved as follows: 5= 2.602+2.398. From this equation, different DL,s could be calculated. For which, the probit value 5, corresponding to a LD50, was replaced by the value of "y" corresponding to the probit value for the doses DL10 (3.72) and DL1 (2.67) Finney (1964).

Substituting the value of "y" for the probit value for the LD50, for example, the equation is: 5= 2.602+1(x). Solving for "x" a value is obtained, whose antilogarithm is the amount in mg of active ingredient per kg of weight of the individuals tested. Finally, the number of deaths caused by different lethal doses was calculated taking into account a weight of 80 kg per person in a population of 1,000,000 inhabitants.

The value of the corresponding members of the equation for the LD50, LD10 and LD1 was obtained by substituting the values in the regression equation y=a+bx, the results of which are shown in Table 1. The table indicates that, based on the LD50 of dimethoate, which is 250 mg per kg body weight, the LD10 was 13.12 mg/kg, while the LD1 was 1.17 mg/kg of weight. Of course, in case the slope of the regression line (b) changes, the result for LDs other than LD50 will be different. This omission in the data sheet makes it impossible to estimate with certainty the lethal effect of insecticides at doses below the LD50. Therefore, the LD50 does not fully express the ability of insecticides to cause death at doses other than the LD50.

DL	y (probit)	a	b	X	X Antilog (mg/Kg)
50	5	2.602	1	2.398	250.0
10	3.72	2.602	1	1.118	13.12
1	2.67	2.602	1	0.068	1.17

Table 1. Values of the members of the equation for the calculation of the LD50, DL10 and LD1, in mg/kg of live weight applying the values of "y" (probit value) of Finney (1964).

It is important to add that the number of deaths caused by the intake of an active ingredient also depends on the number of consumers. As the number of consumers increases the number of deaths increases. Table 2 shows the number of deaths that would be caused by the intake of three different doses (LD50, LD10 and LD1) in a population of 1,000,000 inhabitants. These calculations are based on the insecticide dimethoate, whose LD50 is 250.0 mg/kg. Ingesting an amount equivalent to the LD50 would cause the death of 500,000 people. Which is unlikely given the high amount of ingestion involved. Instead, an intake of 13.12 mg/kg would cause 100,000 deaths. Finally, the intake of 1.17 mg/kg would cause 10,000 deaths in a population of 1,000,000 inhabitants. This is equivalent to the intake of 93.6 mg of active ingredient for every 80 kg person. Which could happen with the consumption of products obtained from crops with a high number of insecticide applications. This exercise shows that insecticides can cause death even at intakes 214 times lower than the LD50. It is clear that the LD50 is not useful to determine risks of death with intakes below the equivalent to the LD50

DL	Dose in mg/kg	% of deaths	Intake/ person of 80 kg.	Deaths/ million inhabitants
50	250	50	20,000	500,000
10	3.12	10	249.6	100,000
1	1.17	1	93.6	10,000

Table 2. Consumers who could die in a population of 1,000,000 inhabitants with the intake of amounts of active ingredient equivalent to the LCs 50, 1 and 0.1.

CONCLUSIONS

Poison amounts below the LD50 also cause death, although at rates less than 50% of consumers. The LD50 value of insecticides only explains the death rate caused by an active ingredient at a single point on the regression line (y=a+bx). In addition, the value of the members "a" and "b" of the regression equation are omitted in the data sheet. For this reason, it is not possible to accurately estimate the lethality of insecticides at doses below the LD50.

Journal of Agricultural Sciences Research ISSN 2764-0973 DOI 10.22533/at.ed.973342312047

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