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A mathematical model for estimating the LC_{50} (or LD_{50}) among an insect life cycle

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ABSTRACT

In this study, a mathematical model is made to estimate the median lethal concentration or dose (LC_{50} or LD_{50}). The model is based on the data of different insecticide groups, where each one is represented by the effect of three insecticides over different orders of insects by using different application technique. The trend of change of the LC_{50} or LD_{50} is observed among the insect life cycle for each group of insecticides. It is shown that for an insecticide group, there is a clear trend for the change of the LC_{50} (or LD_{50}) when going from an age stage to another. That trend is simulated for each group to predict the LC_{50} or LD_{50} at an age stage by knowing it at another stage and method of treatment used.

Keywords: Mathematical modeling, insecticide groups, LC_{50}, LD_{50}, application technique.

INTRODUCTION

Resistance of insect pests to different insecticide groups is the most serious problem in insect pest control. Resistance can develop to virtually any human, animal and crop protection product that is designed to kill pests. The likelihood of resistance occurring and the speed with which it develops depends on a combination of factors that make up the “selection pressure” (Georghiou and Taylor 1977a, b). These factors include (a) the biology and ecology of the pest, (b) how toxic and persistent a pesticide is and (c) the frequency of product use. Once a pest has developed resistance to one pesticide it may also be “cross-resistant” to other pesticides that have the same mode of action. In rare cases, a pest can develop “multiple resistances” to more than one class of pesticide with different modes of action (Lo *et al.* 2000).

The development of organochlorine, organophosphate, carbamate and pyrethroid resistance in different insect groups (Sparks 1981, Wolfenbarger *et al.* 1981), and reports of increased IGR and plant extracts tolerance reported. In addition to resistance problem presence of cross-resistance between the insecticides from different groups such as pyrethroids and DDT(Ahmad and McCaffery 1988). Also a resistance of lepidopteron insects to teflubenzuron, tebufenozide, bifenthrin, and lambda-cyalothtin reveals a cross-resistance to these different insecticides (Sauphanor *et al.* 1998). Resistance in *B. tabaci* is known to be multi-factorial, based on both enhanced detoxification of insecticides and modifications to three of their major target proteins: (1) Acetyl- cholinesterase (AChE), targeted by organophosphates (OPs) and carbamates. (2) The GABA-gated chloride-ion channel, targeted by cyclodienes. (3) The voltage-sensitive sodium channel involved in knockdown resistance (kdr) to pyrethroids (Denholm *et al.* 1998).

Estimation of median lethal concentration or dosage (LC_{50} and LD_{50} respectively) is very valuable. LC_{50} or LD_{50} is indicator to the level of resistance of population response to pesticides. So in this study we focused on estimation of this term by using mathematical models.

In this study a mathematical simulation has been presented for different insecticides groups, which were represented by three insecticides from each group. Then study of their effect on the different insect stages of various insect orders by using the most common methods of exposure at different unites of insecticide concentrations or doses. The importance of the model is that it allows us of predicting the variation of response of different stages (egg, immature stages and mature stage) of various orders to insecticides by using different methods of exposure.

The data were fitted to continuous curves to enable the process of predicting LC_{50} or LD_{50} of certain stage by knowing LC_{50} or LD_{50} and of others at the same technique of exposure.

MATERIAL AND METHODS

Here we describe our mathematical model and the approach taken in its analysis. First, we provide a brief perspective on the insecticides resistance problem. Second, we illustrate in details the general notes about the behavior of changing of the LC_{50} from age stage to another for each group of insecticides. Finally, the programming, computation and analysis of the model are described.

For estimation of LC_{50} or LD_{50} we use in this paper one method of exposure as example, it is topical method for bio-insecticides.

Topical technique: Test-material solutions were applied by topical application to test insects. The test insects were anesthetized by using suitable method to insects used. Then, insecticide dilutions were applied to the ventral abdomen, thorax, between mesothoracic coxa or just behind the head on the ventral side of insect. One micro liter of test-material solution containing the appropriate concentration of insecticides was applied to stage of insect used by a standard digital micrometer syringe and the 24 h mortality was subjected to determine LC_{50} and LC_{90} values (Gouamene-Lamine *et al*. 2003, Lorini and Galley 1998, Meink *et al*. 1998, Nathan *et al*. 2008, Ugurlu and Gurkan 2007, Wing *et al*. 2000 and Wright *et al*. 2000).

Table 1: showing LD_{50} values of response of Lepidoptera, coleoptera and hemiptera when exposed to bio-insecticides by topical technique.

Groups \ Stages	Egg	Larva	pupa	Adult
	ppm			
Imidacloprid (Lepidoptera)	[24.64]	[0.125]	[116]	[2.94]
Imidacloprid (Coleoptera)	[18.3]	[0.074]	[30.3]	[2.47]
Spinosad (Lepidoptera)	[32.50]	[0.193]	[252]	[2.0]
Spinosad (Coleoptera)	[9.8]	[1.069]	[161.244]	[2.66]
Indoxacarb (Lepidoptera)	[16.36]	[0.154]	[35.46]	[4.29]
Indoxacarb (Coleoptera)	[39.9]	[6.45]	[242.92]	[17.8]
	Egg	Nymph		Adult
	µg/g			
Imidacloprid (Hemiptera)	[16.3]	[0.46]		[3.4]
Spinosad (Hemiptera)	[200]	[10.95]		[69.9]
	ppm			
Indoxacarb (Hemiptera)	[84]	[0.33]		[2.32]

Ref: (Abaza 2008, Alves *et al* 2008, El-Dewy 2006, Fang *et al* 2008, Gouamene-Lamine *et al* 2003, Herk *et al* 2008, Khedr 2005, Lambkini *et al* 2007, Lucas *et al* 2004, Medina *et al* 2001, Satpute *et al* 2007, Scharf *et al* 2000, Tillman *et al* 2001, Wang *et al* 2006, Wang *et al* 2007,Wing *et al* 2000).

General notes about the data

We stress on the following important notes that will constitute a guideline for choosing the assumptions of the mathematical model:

- Despite the differences between the values of the LC_{50} for two kinds of insecticides or insects, they have a similar trend for the variation of the LC_{50} when going from a stage to another.
- We can't conclude that the LC_{50} is different in a group of insects than another one. The values are varying with no observed trend along a group of insects.
- The only observed trend is in the change of the value of the LC_{50} when moving from a stage to another one along the life cycle of the insect. All the relatively small or large values of *m* are within less than 3 standard deviations about the mean, i.e., they can't be considered extreme values.
- All the relatively small or large values of m are within less than 3 standard deviations about the mean, i.e., they can't be considered extreme values.
- The differences between the relatively small or large values of *m* and the mean (measured in standard deviations) is always less than the differences between the corresponding values of the $LC_{50.}$
- A parameter is suggested to describe the change of the LC_{50} when going on the life cycle from a stage to another stage. We call it "*m*". It simply represents the ratio of the difference between the value of the LC_{50} in the second stage and the first stage to the LC_{50} of the first stage.
- For example *m* [egg, Larvae] = $\dfrac{LC50\,Larvae - LC50\,egg}{LC50\,egg}$
- All the relatively small or large values of *m* are within less than 3 standard deviations about the mean, i.e., they can't be considered extreme values.
- The differences between the relatively small or large values of *m* and the mean (measured in standard deviations) is always less than the differences between the corresponding values of the $LC_{50.}$

Assumptions of the mathematical Model

To get a mathematical model that is consistent with the data collected above, we follow the following assumptions,

1- The model categorized the data according to insecticide groups.
2- No distinguish is made among different groups of insects.
3- There is a clear trend of change of the LC_{50} along a life cycle.
4- The variable *m* is assumed to be normally distributed for each insecticide between two age stages.
5- For each group of values of *m* corresponding to transformation between two stages for an insecticide, the mean and standard deviation are used to calculate confidence intervals to estimate the LC_{50} at an age stage given the LC_{50} of the previous stage along the life cycle of the insect.

RESULTS AND DISCUSSION

Calculations of the Model

In the following table, we illustrate the details of the calculations required for the model. Consider the following table of the LC_{50} values of an insecticide for two different stages *a* and *b*.

Stage a	Stage b
a_1	b_1
a_2	b_2

⋮	⋮
a_k	b_k

- We complete the table as follows,

Stage a	Stage b	*m*
a_1	b_1	$\frac{b_1 - a_1}{a_1}$
a_2	b_2	$\frac{b_2 - a_2}{a_2}$
⋮	⋮	⋮
a_k	b_k	$\frac{b_k - a_k}{a_k}$

- Then we calculate,

$\overline{m}$ = mean of *m* values

σ = standard deviation of *m* values

  - **Now, given that the LC_{50} at the stage a equals x, it is required to get the LC_{50} at the stage b**
    - We calculate a 1-α confidence interval (α = 0.01, 0.05, 0.1,…), using the following formula
    - LC_{50} at stage b is assumed to be (1-α)% confident in the interval $x(1+[\overline{m} \pm e])$
    - Where *e* is simply the radius of the tow sided confidence interval of a normally distributed variable.
    - For a sample of *k* (<30) elements, whose standard deviation is σ, the value of "*e*" for a 1-α confidence interval is given by

$$e = \frac{\sigma t_{k-1,\alpha/2}}{\sqrt{k}}$$

Application to the case of bio-insecticides, topical exposure

In what follows, the simulation process is illustrated through an example showing the application of the above technique to table 1 of LD_{50} values of response of Coleoptera, and Lepidoptera when exposed to bio-insecticides by topical technique.

In table (2), the values of m between the different age stages are calculated as well as their means and standard deviations as shown below.

Table 2: showing $m, \overline{m}$, and σ values estimated from data in table (1) by using our model equation.

	Egg -> Larva	Egg -> Pupa	Larva -> Pupa	Egg -> Adult	Larva -> Adult	Pupa -> Adult
Imidacloprid (Lepidoptera)	-0.994	3.70	927	-0.88	22.52	-0.974
Imidacloprid (coleoptera)	-0.995	0.655	408.4	-0.865	32.37	-0.918
Spinosad (Lepidoptera)	-0.994	6.75	1304.6	-0.938	9.362	-0.992
Spinosad (coleoptera)	-0.890	15.45	149.8	-0.728	1.488	-0.983
Indoxacarb (Lepidoptera)	-0.990	1.167	229.25	-0.737	26.85	-0.879
Indoxacarb	-0.838	5.088	36.66	-0.553	1.75	-0.926

(coleoptera)						
$\overline{m}$	-0.95	5.46	509.28	-0.783	15.723	-0.945
σ	0.068	5.40	499.6	0.14	13.3	0.044

- Thus for example, for a 95% confidence interval where k = 6 (number of data), we find from the t-table that $t_{5,0.25}$ = 2.571.
- Then to estimate the LD_{50} at the larva state knowing that its value is *x* at the egg state, we substitute the formula LD_{50} (Larva) = $x(1+[\overline{m}\pm e])$
- Where $e=\dfrac{\sigma t_{k-1,\alpha/2}}{\sqrt{k}} = \dfrac{0.068(2.571)}{\sqrt{6}}=0.0714$
- Thus the LD_{50} at the Larva stage is 95% confident to lie within the interval $x(1+[\overline{m}\pm e])=x(1-0.95-0.0714,1-0.95+0.0714)=x(-0.02,0.121)$
- Of course the negative value is rejected, so all we can say about this case is that the Larva LD_{50} is expected to be less than 0.121*x* with 95% confident.
- For example if the LD_{50} at the egg stage is 15, it will be estimated with 95% confident to be less than 0.121(15) = 1.815 in the Larva state.
- As estimated in this example we can predict any LC_{50} or LD_{50} to any stage at by knowing LC_{50} or LD_{50} to other stage and the method of exposure used.

It is to be noted that, if we were seeking a point estimate of the LC_{50} rather than an interval estimate (as in our case) the formula of the LC_{50} at the b-stage would be just $x(1+\overline{m})$, but it would be of course less accurate.

This work is a first trial for predicting the LC_{50} of insecticides along an insect life cycle. We hope that future work be carried for each insecticide group seeking a more accurate and closer values for the mean and the standard deviation.

In the case that a study collects a sample of more than 30 results of the same unit, the t-distribution will be replaced by the z-distribution.

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ARABIC SUMMARY

موديل رياضى لتقدير LC_{50} او (LD_{50}) بين دورة حياة الحشرة

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في هذه الدراسة ، تم إجراء نموذج رياضي لتقدير التركيز أو الجرعة المميتة للنصف LC_{50} او(LD_{50}). هذا الموديل اعتمد على بيانات من مجموعات مبيدات مختلفة، حيث ان كل مجموعة منها ممثلة بتأثير ثلاث مبيدات على رتب مختلفة من الحشرات باستخدام طرق تطبيق مختلفة. وقد لوحظ ان هناك نزعة فى تغير LC_{50} او(LD_{50})خلال دورة حياة الحشرة لكل مجموعة من المبيدات . ولقد تبين ان كل مجموعة من المبيدات لها

نزعة واضحة لتغير LC_{50} او(LD_{50}) عند الانتقال من مرحلة عمرية الى اخرى . تلك النزعة هى محاكاة تستخدم للتنبؤ ب LC_{50} او(LD_{50}) عند مرحلة عمرية وذلك بمعرفتهما عند مرحلة عمرية اخرى وطريقة المعالجة المستخدمة.