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FITTING THE GOMPERTZ FUNCTION TO DOSE-RESPONSE DATA OF LARVAL TICK POPULATIONS

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ABSTRACT

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Samples of 6, 1st generation larval populations of *Boophilus decoloratus*, originating from field collected females, were subjected to increasing doses of the organophosphate acaricide, Dioxathion. The dose-response relationship for 3 populations showed random heterogeneity, while systematic deviations from the linear probit lines were observed for the other 3 populations. Logistic and Gompertz regressions were also fitted for all 6 populations.

Probit regressions fitted best for 2 populations exhibiting heterogeneous responses. The logistic regression fitted best for 1 population with heterogeneous responses and 1 population with systematic deviating responses. The Gompertz regression fitted best for the 2 remaining populations exhibiting systematic deviating responses.

The Gompertz function may be useful in describing the dose-response relationship obtained for certain acaricidal toxicity tests.

INTRODUCTION

Routine toxicity tests for acaricides are normally evaluated by means of probit analyses (Finney, 1971; Nolan, Roulston & Wharton, 1977), or by fitting a logistic curve (Solomon, 1983). A homogeneous response, which a susceptible tick population normally exhibits, is necessary for these analyses. The lethal dose (LD) of 50 %, 95 % or 99 % of the population may then be accurately determined to evaluate the effectiveness of acaricides or the degree of resistance of populations.

One of the main problems in analysing toxicity tests is the occurrence of heterogeneous response of the tick larvae to increasing doses of acaricide. This may be caused by one or more factors, such as differences in the age of individuals or by inaccurate test procedures (Nari, 1981). However, larvae, sampled from natural environments where exposure to acaricides has occurred, more often than not exhibit inherent differences in susceptibility of individuals and/or degree of resistance of the population. This leads to unrectifiable heterogeneous responses during toxicity tests and accurate assessment of the efficacy of an acaricide or the extent of the resistance developed becomes difficult.

Such heterogeneous response usually results in a poor fit of the probit regression, and consequently unreliable LD values are obtained. Finding a response curve which fits heterogeneous data (indicating systematic deviations from a probit line) is therefore desirable. This is especially true if resistance of a population to an acaricide is suspected and if it must be determined how resistant that population has become. Such resistance is usually determined by comparing the dose-response regression (and/or one or more LD values) for the presumably resistant population with that for a susceptible population (Baker, 1982; Solomon, 1983).

Vieira & Hoffmann (1983) mentioned that the Gompertz function may lead to best fitting of response data where the inflection point is smaller than 0,5, in constrast to the inflection point of 0,5 for the probit and logistic regressions. They demonstrate fitting this function for 1 example on the influence of pupal age of fruit flies on the radiosensitivity to increasing doses of gamma-irradiation.

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It is possible that this curve may also be useful for toxicity tests, using a single series of doses of an acaricide for which systematic deviations from a probit line are evident. One aim in this paper is to compare the usefulness of the Gompertz curve with probit and logistic regressions for such cases.

MATERIALS and METHODS

The responses from 6 routine toxicity tests with the organophosphate, Dioxathion, for *B. decoloratus* larvae, the 1st generation offspring of females sampled from natural populations, were used to compare the fit of the probit, logistic and Gompertz regressions. For each toxicity test 6 doses were applied and reasonably representative ranges of mortalities (between 7,1 and 99,2 %) were obtained. Larvae were exposed to the acaricide doses by means of the filter paper method as described by Shaw (1966).

Probit analyses were carried out using the program (LSTATS)P/PROBAN, writting by the second author, while the logistic and Gompertz regressions were fitted by means of the program (LSTATS)P/STKROMME, written by S. H. C. du Toit and A. Herbst, S.A. Human Sciences Research Council[1].

The probit line is defined by $y = a + bx$, were y is the empirical probit and x is the $\log_{10}$ dose. The logistic curve is defined by the equation $y = a/(1+br^t)$, for $a > 0$ and $0 \leq r \leq 1$, where y is the percentage mortality, a is the saturation value for y, b is a function of the potential increase in toxicity, r is related to the growth tempo and t is the dose. The Gompertz curve is defined by the equation $y = ae^{-br^{**}t}$, for $a > 0$, $b > 0$, $0 \leq r \leq 1$, where y is the percentage mortality, a is the saturation value for y, b is a function of the potential increase in toxicity, r is related to the growth rate and t is the dose. The Gompertz curve is not symmetric about its point of inflection as is the case for the probit and logistic curves.

The comparisons of the 3 regression methods were based on the associated probability of the F value for fit of the regressions and on the derived LD50, LD90 and LD95 values.

[1] Directorate of Biometric and Datametric Services, Department of Agricultural Development for use on a Unisys B7900 computer

RESULTS AND DISCUSSION

The results of 3 toxicity tests for which the test larvae showed random heterogeneous responses (RH 1, RH 2 and RH 3) after subjection to probit analyses, are presented in Fig. 1. The chi-squared values for all 3 analyses were highly significant ($P < 0,001$). No clear systematic deviations from the linear probit lines were observed. The results for 3 other tests with systematic deviations (S 1, S 2 and S 3) are presented in Fig. 2. The chi-squared values for these 3 probit analyses were also highly significant ($P < 0,001$), indicating heterogeneous responses, but graphical inspection indicated possible systematic deviations from the linear probit lines. In these tests the rate of increase of response for the smaller doses is faster than expected and a marked point of inflection, is evident after which the rate of increase decreases dramatically.

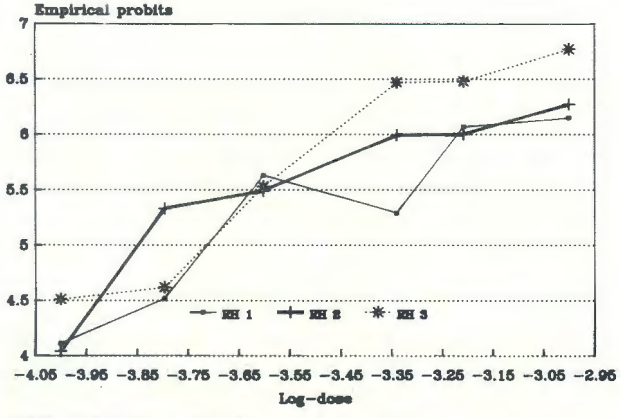

FIG. 1 Probit analysis for populations showing random heterogeneity

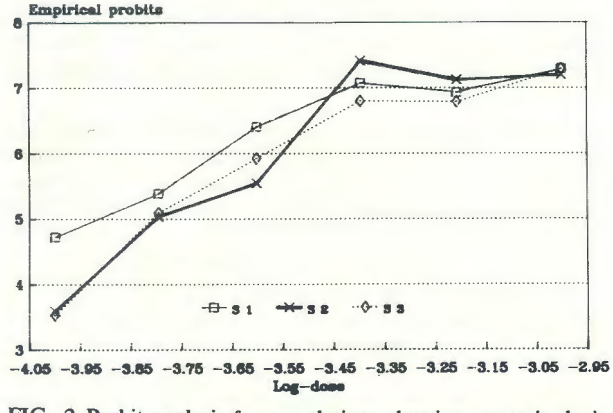

FIG. 2 Probit analysis for populations showing systemic deviations

The F value for fit of the 6 regressions and the associated probability for each toxicity test are given in Table 1. The degrees of freedom for the probit regressions were 1 and 4, and those for the logistic and Gompertz regressions 3 and 3.

The LD50, LD90 and LD95 values calculated from the regressions are given in Table 2. For 3 logistic and 2 Gompertz regressions, the saturation point (a) was lower than some of the required LD values, and the latter could not be calculated.

Based on the probability for fit, the probit regressions which fitted best are presented in Fig. 3, the best fitted logistic regressions in Fig. 4, and the best fitted Gompertz regressions in Fig. 5.

TABLE 1 Goodness of fit of regressions

	Probit	Logistic	Gompertz
Random heterogeneity			
RH 1 F value	26,29	7,68	7,47
Probability	**0,006849**	0,064054	0,066380
RH 2 F value	31,83	15,08	17,93
Probability	**0,004859**	0,025829	0,020281
RH 3 F value	49,02	65,72	41,32
Probability	0,002191	**0,001783**	0,006122
Systematic deviations			
1 F value	30,91	681,59	223,54
Probability	0,005125	**0,000095**	0,000504
S 2 F value	21,50	23,03	37,45
Probability	0,009760	0,014229	**0,007064**
S 3 F value	34,27	47,59	126,81
Probability	0,004248	0,004982	**0,001172**

Bold-figured probabilities indicate the best fit

TABLE 2 Lethal dosage values (ppm) for the regressions

	Probit	Logistic	Gompertz
Random heterogeneity			
LD50	**23**	19	20
RH 1 LD90	**97**	a=79 %	a=82 %
LD95	**146**	a=79 %	a=82 %
LD50	**16**	19	14
RH 2 LD90	**71**	a=82 %	a=83 %
LD95	**109**	a=82 %	a=83 %
LD50	16	**17**	17
RH 3 LD90	48	**38**	41
LD95	66	**55**	56
Systematic deviations			
LD50	12	**12**	12
S 1 LD90	28	**24**	25
LD95	36	**29**	31
LD50	18	18	**17**
S 2 LD90	35	31	**32**
LD95	42	36	**38**
LD50	17	19	**16**
S 3 LD90	35	24	**27**
LD95	42	a=94 %	**34**

a = Saturation point or asymptote

Bold-figured LD values are those for the best fitted regressions

The probit regression fitted best for the population RH 1, while the fit for the logistic and Gompertz regressions where non-significant at $P = 0,05$. For RH 2, the probit regression also fitted best, with poorer fit (although significant at P =

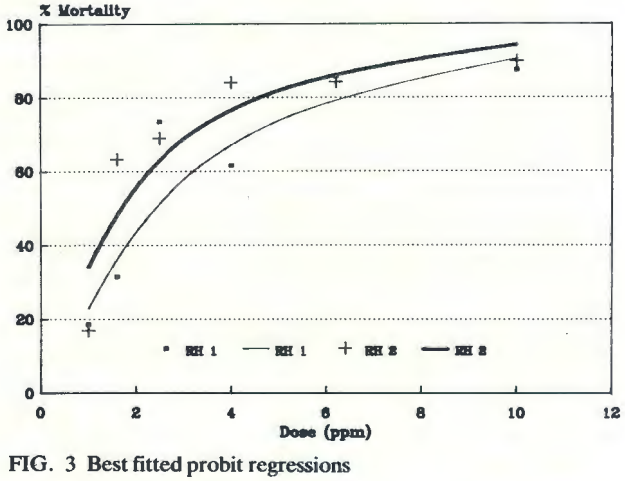

FIG. 3 Best fitted probit regressions

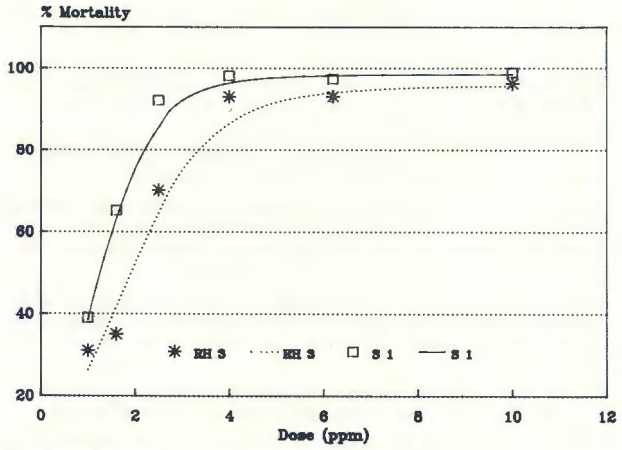

FIG. 4 Best fitted logistic regressions

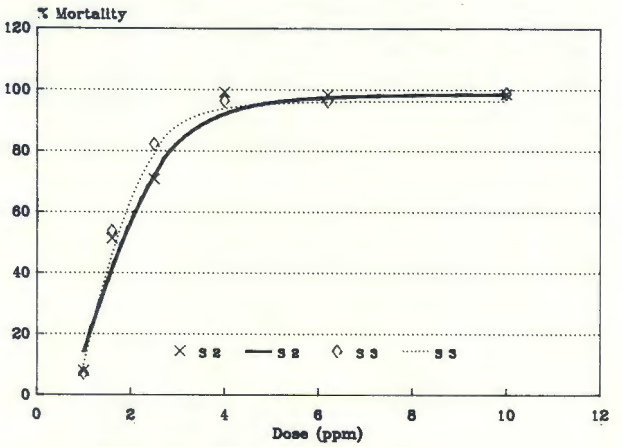

FIG. 5 Best fitted Gompertz regressions

0,05) of the Gompertz and logistic regressions. For RH 3, the logistic regression fitted slightly better than the probit regression, while the Gompertz regression also fitted reasonably well (Table 1).

For the population, S 1, the most satisfactory fit was obtained with the logistic regression, followed by the Gompertz and probit regressions. For S 2, the best fit was obtained with the Gompertz regression, but this fit was only slightly better than that for the probit regression. The logistic regression fitted poorly, although significantly at $P < 0,015$. For S 3, the fit of the Gompertz regression was superior to both the fit of the probit and logistic regressions, which also fitted approximately equally well and significantly at $P < 0,005$ (Table 1).

In general, the probit and logistic regressions fitted best when random heterogeneous responses were evident. Where systematic deviations were evident, better fits were obtained with the Gompertz and logistic regressions than with the probit regressions.

It is evident (Table 2), that the LD50 values derived from the 3 regressions did not differ materially. This was as expected, because the LD50 values represent the midpoints of the regressions and can to a certain extent be independent from the slope of the response regressions. The LD50 values are usually of limited value when populations for which resistance is not very marked are compared with susceptible populations (Van Ark, 1983).

When fitting logistic or Gompertz regression, the higher LD values (such as 90, 95 or 99) can only be calculated if the saturation point (a) is higher than the required LD value. Low saturation points were encountered for the poorly fitted logistic and Gompertz regressions of the populations (RH 1 and RH 2), showing random heterogeneity of response (Table 2). Although the logistic regression for S 3 fitted fairly well, the saturation point was below 95 %. Generally, the best fitted regression for each population resulted in the lowest LD90 and LD95 values. This is logical, considering that a linear relation tends to overestimate these values when a true curvilinear relationship is evident, as demonstrated for the examples. The same is true for curvilinear regressions fitted to true linear relationships.

To obtain the most reliable results of a toxicity test it is obvious that the regression which best describes the responses to an acaricide should be used. Selecting such a regression is a complex procedure. The obtained responses should first be subjected to conventional probit analysis. If homogeneous responses are evident (a non-significant chi-squared value), the analysis is accepted as such. If heterogeneous responses are obtained, the results can be inspected to determine if the heterogeneity is due to random heterogeneous responses or systematic deviations form the linear probit regression.

It is often difficult, however, to separate random heretogeneous response to doses from responses that show clear systematic deviations, especially if a limited number of doses have been used. Fitting a 2nd degree polynomial to responses sometimes confirms the latter systematic deviations. The successful fit of such a polynomial, however, depends largely on the variation of the responses and the number of responses obtained. On failure of fitting a significant polynomial regression, evidence of systematic deviations can be obtained graphically by comparing observed and expected responses, or from residuals. Plotting % mortality against dose may aid in this procedure. Curves for random heterogeneity tend to increase gradually and indicate probit regressions as depicted in Fig. 3 and to a lesser extent for RH 3 in Fig. 4. Curves for systematic deviations tend to have a more clearly defined point of inflection and indicate that logistic and/or Gompertz regressions should be fitted (Fig. 4 & 5).

After fitting these regressions, the regression which fits best (with the smallest probability) can be accepted. It must be emphasized that the larger the number of dose-response values the more accurate the fit of the regression will be, especially if a curve is to be fitted. If curvilinear response is expected, it is advisable to use as many doses (at least 10) of the acaricide as is practicably possible. Blocking for factors, such as age and development stage of test individuals and increasing the accuracy of the test procedures, will also reduce heterogeneity of response (Van Ark, 1983) and consequently increase the accuracy of the fit of a regression.

Inclusion of doses which will result in mortalities near zero and near 100 % is also recommended. Doses at which responses of exactly 0 % and 100 % will be obtained are, however, difficult to determine. If such doses seem to be too low or too high respectively, they should not be included in an analysis, because they may exert unwanted influence on the shape of the regression. Fitting regressions to data representing only part of the whole possible dose-response relationship is inadvisable, as this may lead to incorrect interpretations.

Comparing the dose-response relationships of different populations especially by means of the slope of the regressions may be problematical. The authors are not aware of any biometrical technique by means of which various curvilinear regressions may be compared. Furthermore, the logistic and Gompertz functions cannot be linearized by means of transformations.

Resistance to acaricides may manifest itself in various ways (Nolan, 1981; Stone, 1981). The fact that the dose-response relationship tends to flatten at higher doses may be an indication of the presence of resistance. The saturation point (a) may therefore be indicative of the extent of resistance of a certain nature. It seems that the Gompertz function may be useful for describing certain relationships. Fitting this regression and also the logistic, however, cannot be carried out as a matter of course and prior careful consideration of the nature of the dose-response data is indicated.

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