

PLOTTING ISOBOLE WITH LOGISTIC REGRESSION

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Background and Aims: Studies concerning interactions between different toxicants are of fundamental interest and practical importance in toxicology. However, there is still no consensus of opinion with regard to the assessment of interaction between agents. We, therefore, should be careful about using the terms additivity, synergism and antagonism, especially where nothing is known about the mechanisms underlying the toxic action. The Loewe additivity model and its extension in the form of isobolographic method are mostly used for assessing the type of combined action in co-exposure experiments. Moreover, practical plotting of an isobole is a non-trivial task.

Methods: We propose to plot an isobole using a logistic regression equation for primary data. In many cases, the outcome of interest is binary (i.e. taking 0, 1 values), and toxicants are continuous (e.g. air pollutant concentrations). By standard calculation, we can get a logistic regression equation $w = f(x, y)$, reflecting the impact of toxicants on objects. The co-exposure of toxicants may manifest itself in a variety of ways, e.g. additive effects, synergism or antagonism. Each of these cases produces some kind of isobole. We can design this plot in 2 steps. Firstly, we calculate disease prevalence w_0 from primary data. Secondly, we find the corresponding isobole solving the implicit equation $w_0 = f(x, y)$.

Results: We have tested this method on various real and simulated data sets, and have come to the conclusion that it is easier and more correct than others. This method of isobole construction may help, with a certain degree of approximation, find isoeffective doses of toxicants (points of intersection of this isobole with the axes).

Conclusions: The isobole plotting method proposed in this report may have some advantages compared to other methods. It has significant stability to outliers, and may be applied to various data sets with minimal preparation.