STATISTICAL ESTIMATION OF DRUG-RECEPTOR MODEL PARAMETERS; COMPARING THE PERFORMANCES OF TRADITIONAL METHODS WITH A NONLINEAR LEAST SQUARES METHOD.

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The Hill plot and Schild plot (traditional methods: TMs) have been used to estimate parameters, such as a dissociation constant (K) and a slope coefficient (N) in drug-receptor model. However, TMs have a disadvantage that they transform response variables and may distort the distribution of experimental errors. It is more straightforward and reasonable to apply a nonlinear least squares method (NLIN) without variable transformation. When using NLIN, appropriate initial values for each parameter must be specified. However, to provide precise estimates of them is quite difficult for pharmacological researchers who are not necessarily accustomed to using NLIN. Therefore, we compared the performance of NLIN with TMs by simulation in order to confirm the superiority of NLIN and provided an easy-to-use method for specifying initial values for NLIN. Although the performance of these methods was almost the same in estimating K, TMs provided remarkable negative biases in estimating N. The estimate of N in NLIN was less biased when the estimates by TMs were used as initial values for NLIN. It is, however, necessary to check whether the estimate by NLIN is reasonable or not, because NLIN sometimes created remarkably outlying estimates. The validity of estimates by NLIN could be checked by comparing them with their initial values. We recommend using NLIN for the parameter estimation in drug-receptor model because NLIN provided less biased estimates.