

Using blepharospasm of the guinea-pig eye as the response to topically applied irritant, the threshold concentration was calculated as the concentration required to produce the response in 50% of a group of animals (TC_{50}). The test was found to be easy to perform, free from tachyphylaxis, to give reproducible values with restricted 95% confidence limits, and to separate irritant materials of relatively close chemical structure.

The flexor response was carried out with decerebrate frogs whose hind limbs were immersed in progressively stronged solutions of irritant. Using withdrawal of the limb as a positive response, the log molar concentration of irritant was plotted against withdrawal time and the curve was extrapolated by fitting a template of a standard curve defined by:

$$C = \frac{1}{1 - e^{-t}}$$

where C = concentration of irritant, and t = withdrawal time. In this way the minimum irritating concentration was estimated. This technique was found to be relatively insensitive, the results were variable and there was evidence of tachyphylaxis.

Depression of the respiratory rate of the mouse, measured by whole body plethysmography, was used to assess the response to aerosols of irritants. The peak depression of respiratory rate was measured for several concentrations, and the threshold value calculated as that producing a 50% depression rate. The test is time-consuming but was found to have all the advantages of the blepharospasm test and appeared the most sensitive.

No single animal test is likely to be completely adequate for screening the relative potency of sensory irritants, but the guinea-pig blepharospasm test offers a simple technique for reliable comparative tests. These may require confirmation using mouse plethysmography and, where appropriate, studies on man.

Results from animal threshold studies may not be a reliable guide to the situation in man, and do not allow the measurement of subjective irritant effects. Thus, for *o*-chlorobenzylidene malononitrile the threshold values were 2.2×10^{-5} M by guinea-pig blepharospasm, 6.0×10^{-8} M by mouse plethysmography and 9.8×10^{-6} M by flexor reflex. In man, we found the TC_{50} for blepharospasm to be 3.2×10^{-6} M and for elicited corneal sensation to be 7.3×10^{-7} M. The human eye appears about 7 times more sensitive to this irritant than does the guinea-pig eye, using blepharospasm as the response. The TC_{50} for sensation on the human tongue was 6.8×10^{-6} M, a concentration 9.4 times that required to elicit corneal sensation. Extrapolation of the data used to obtain TC_{50} values in man in the form of log probit plots may be of value for predicting incapacitating concentrations of irritant materials.

The assessment of β -adrenoceptor blocking compounds in the conscious dog (T)

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