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Ocular irritation tests

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Investigations on the potential of substances to cause damage to the eye cover numerous products used in industry, agriculture and medicine. The more important considerations in ocular irritation tests are discussed.

Observations are required on both formulations and active ingredient. The latter is tested as undiluted liquid or solid, and at serial dilutions to determine the maximum concentration having no undesirable effects. Groups of 6 or more animals are required. The rabbit is frequently used, but where possible the response should be checked against primates (Beckley, Russell & Rubin, 1969).

Two important factors are the solvent and the volume instilled (Ballantyne, Gazzard & Swanston, 1972). Non-irritant solvents without effects on intraocular tension are required; saline, polyethylene glycol 300, propylene glycol and glyceryl triacetate are examples. A convenient volume is 0·1 ml.

Eyes are examined and photographed at 10 min, 1, 6 and 24 h, and thereafter daily for 2 weeks. Macroscopic observations should be supplemented with biomicroscopy and fundoscopy. Cumulative single figure scoring systems, like that of Draize (1959), involve calculating a single average of all effects observed, and incorporate a heavy bias on corneal pathology. Such scores are uninformative about responses of individual tissues and thus, a specific Draize score could result from two entirely different reactions. Scoring bias ignores the significance of some effects; for example, severe contracture of the eyelids may be equally as serious as keratitis. In our laboratories means for each effect, scored on a 5 point scale, are calculated for the group at each inspection period. Such mean scores, recorded as a function of time on tables or graphs, are easier to interpret and more meaningful than cumulative weighted scores. Thus, they readily allow comparison of the effects of varying concentrations (Fig. 1) and facilitate comparison of particular effects produced by different oculotoxic drugs.

Macroscopic observations should be supplemented with terminal and sequential histopathology. Any advantages of the cup-aspirator technique (Buehler & Newmann, 1964) require confirmation, but applanation tonometry may be an additional valuable technique in ophthalmic toxicology (Ballantyne, Gazzard & Swanston, 1972).

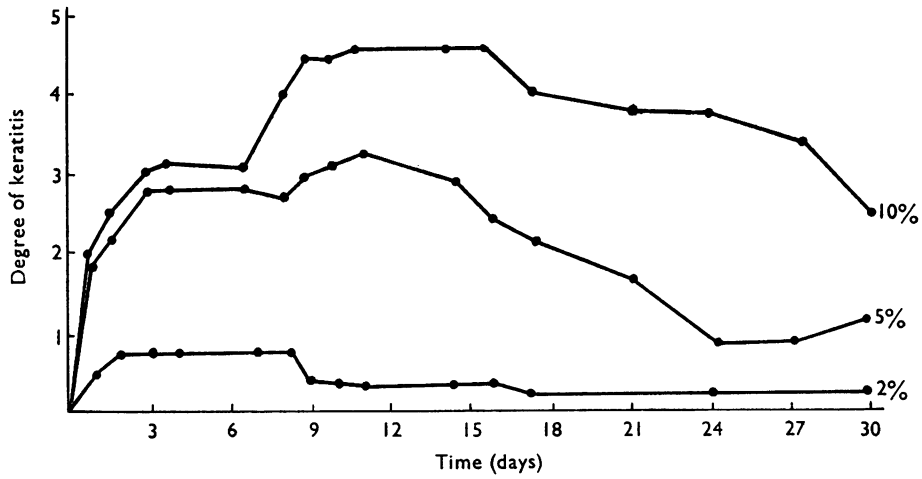

FIG. 1. The effects of ω-chloracetopenone on the rabbit cornea, plotted to show the effects of increasing concentrations. The degree of corneal damage is represented on a 5-point scale varying from slight swelling of the cornea with minimal acute inflammatory cell infiltration (point 1) to gross opacification with deformity of the cornea (point 5).

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Application of an inexpensive analogue computer for the continuous determination of airways dynamic compliance and resistance

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An on-line analogue computer was described by Dennis, Douglas, Casby, Stolwick & Bouhuys (1969) for determination of compliance and resistance. Certain defects in their design were reported by Giles, Finkel & Mazurowski (1971). Douglas, Dennis, Ridgeway & Bouhuys (972) have made available a new circuit design.

The new computer has been constructed in our laboratories and adapted for use with Devices pen recorders. The output signals are also led, via calibration units, to provide continuous visual display of compliance and resistance in absolute units.

During experiments, flow ($\dot{V}$), tidal volume (V), and transpulmonary pressure (P) signals are fed continuously into the computer. Values of dynamic compliance are computed for each breath at points of zero flow from instantaneous volume