Mepacrine uptake by granulocytes *in vitro*

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Purified horse granulocytes when incubated *in vitro* with mepacrine show decreased random migration (Palmer & Weatherall, 1977) and decreased phagocytosis (Baker, Trist & Weatherall, 1976). It has been reported that mepacrine is concentrated by some mammalian tissues and in particular by leucocytes (Parmer, 1948). Also, Allison & Young (1964) showed that mammalian cells in culture selectively accumulated mepacrine into lysosomes.

Concentration of mepacrine by granulocytes has been confirmed both chemically and by fluorescent microscopic observation. When granulocytes were incubated with mepacrine (10 μM to 100 μM), after 30 min the cellular concentration was some 200- to 500-fold greater than that in the suspending media. The appearance of mepacrine within the granulocyte could be observed by fluorescence microscopy. It will be shown that as time proceeded numerous vesicles within the cell became fluorescent and fused to become larger vacuoles.

References

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A screen for assessing the audio-toxic potential of aminoglycoside antibiotics

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When this study commenced, three main approaches —histological, electrophysiological and behavioural— had been used to assess, in animals, the ototoxic potential of drugs. From the screening point of view, the methods employed all suffered from disadvantages—they were complex and time-consuming or required large quantities of compound or needed specialized and expensive equipment. The objective, therefore, was to develop a simple, quick, reliable and valid method of assessing the auditory toxicity of aminoglycoside antibiotics which required the minimum of compound and could act as a screen.

It was based on Preyer's reflex in Redfern strain guinea-pigs used approximately 48 h after birth and allocated on a sex/weight basis to groups containing 4 to 7 animals. Each animal was weighed and had its auditory parameter measured each day, just prior to treatment, for the duration of the experiment—20 days unless death or deafness occurred earlier. Deafness was taken as the absence of Preyer's reflex at the maximum volume setting available on the apparatus for each frequency used. Sound was generated by a Levell R.C. oscillator (Type T.G. 200) which delivered a pure sine-wave signal of adjustable frequency to an amplifier/control unit and emitted by a Goodmans Magnum K2 speaker system in pulses of 0.2 s duration at 1 s intervals. The auditory parameter—threshold sound intensity (decibels (dB) at 1 ft) for Preyer's reflex—was measured by positioning each animal with its ears 30 cm from the speaker. The volume of sound—frequency 2 KHz—was adjusted to elicit Preyer's reflex and then reduced until external ear movement ceased. This volume setting was converted to decibels using a calibration chart and taken as the threshold sound intensity. The process was repeated at 4, 8, 12 and 16 KHz.

Graphs of the mean threshold sound intensity for Preyer's reflex at 12 KHz against time in days provided the most convenient assessment of auditory toxicity. The results obtained with gentamicin, kanamycin A, kanamycin B, neomycin, streptomycin, cephaloridine and potassium propicillin, administered subcutaneously, indicated that: frequent, regular exposure to sound did not result in habituation; the auditory toxicity of those aminoglycosides recognized to be audio-toxic could be reliably and reproducibly detected; the relative auditory toxicities obtained were consistent with reported data; the numbers of days required to produce deafness represented an advance over the times reported in the literature; the relative audio-toxic potential of novel aminoglycosides could be assessed with a maximum of 1.5 g of compound. As Preyer's reflex was simple to use, the method developed was considered to fulfil the initial objective and has been used successfully as a screen.