

reductions in the score (Fig. 1B). These decreases are also dose-related ( $F = 8.21$ ,  $df = 29$ ,  $P < 0.01$ ). The 10% polysorbate 80-saline vehicle has no effect on the severity of audiogenic seizure, as indicated by lack of change in score (Fig. 1 A, B).

The median effective dose (ED<sub>50</sub>) for complete suppression of audiogenic seizure was determined for  $\Delta^8$ - and  $\Delta^9$ -THC according to the method of Litchfield & Wilcoxon (1949). The ED<sub>50</sub> and corresponding 95% fiducial limits for  $\Delta^8$ -THC and  $\Delta^9$ -THC are 6.5 mg kg<sup>-1</sup> (3.5 — 11.8) and 3.3 mg kg<sup>-1</sup> (2.0 — 5.5), respectively. Despite the fact that the ED<sub>50</sub> of  $\Delta^8$ -THC is almost twice that of  $\Delta^9$ -THC, statistical comparison of the relative potency of the two tetrahydrocannabinols (Litchfield & Wilcoxon, 1949) indicate that the ED<sub>50</sub>s are not significantly different from each other ( $P > 0.05$ ).

The data presented clearly show that  $\Delta^8$ -THC and  $\Delta^9$ -THC have anticonvulsive activity and that such activity is dose-related. Furthermore, the anticonvulsant potencies for the two cannabinols are similar in the test system used.

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## The fluorescence of paracetamol—a re-examination

During a recent literature search on the physical and chemical properties of paracetamol, it became apparent that the only paper in which the fluorescent properties of this pharmaceutically important compound had been reported in any depth was that of Nang & Pitet (1965), although Child, Bedford & Tomich (1962) had earlier described paracetamol as fluorescent.

In view of the paucity of published work on the fluorescence of paracetamol, attempts were made in our laboratories to repeat some of the work of Nang & Pitet.

Freshly prepared solutions of paracetamol B.P. in 10<sup>-3</sup>M sodium hydroxide (3 × 10<sup>-3</sup>M), in 1% aqueous ethanol (50 μg ml<sup>-1</sup>), and in ethanol (3 × 10<sup>-3</sup>M) were examined for fluorescence with a Baird Fluorispec SF1 spectrofluorimeter equipped with an EMI 9781B photomultiplier. With the emission monochromator set at 400 nm, the excitation monochromator was adjusted until a maximum meter response was noted. With the excitation monochromator set at this maximum, the emission monochromator was adjusted to a maximum meter response. The fluorescence excitation and emission spectra were then recorded in a conventional manner.

For both the alkaline and aqueous ethanol solutions of paracetamol, a very weak emission was observed at 405 nm with an excitation maximum at 355 nm. An identical response was obtained from the solvents alone. Further examination showed

that the spectra observed for both the alkaline and aqueous ethanolic solutions of paracetamol were a result of Raman scattering of water, which shows a maximum intensity at approximately 390 nm with incident radiation of 340 nm, and a peak of similar intensity at approximately 410 nm, with excitation at 360 nm. The wavelengths of excitation and emission of the latter correspond to those observed for the alkaline and aqueous ethanol solutions of paracetamol.

For the ethanolic solution of paracetamol, a somewhat more intense fluorescence was observed, identical to that obtained with ethanol alone. In this instance, the fluorescence could be attributed to the presence of impurities in the ethanol used.

The absorption spectrum of paracetamol was recorded for  $10^{-2}$ ,  $10^{-3}$  and  $10^{-4}$ M solutions of paracetamol in 1% aqueous ethanol. In none of the samples was absorption observed at wavelengths greater than 310 nm. The longest absorption wavelength occurred at 244 nm, with a slight shoulder at 280 nm. Since it is necessary to correct fluorescence excitation spectra for the variation in the intensity of the excitation radiation, the uncorrected excitation spectrum will not be comparable to the absorption spectra. However, a fairly close relation between an absorption maximum and the excitation maximum would be expected. The use of high concentrations of paracetamol showed the absence of any low-intensity absorption that could have been assigned to a low energy  $n\pi^*$  transition.

In view of these findings, a further screening for fluorescence was made with excitation at 250 nm. No fluorescence was observed for any of the solutions examined.

On the basis of the findings reported here, it is concluded that paracetamol is non-fluorescent, and that the excitation and emission characteristics reported by Nang and Pitet were a result of Raman scatter, or were due to the presence of impurities in the paracetamol used.

Additional doubts as to the validity of the results obtained by these authors arise from their report of the fluorescence of solutions of acetanilide, a compound that had earlier been reported to be non-fluorescent by Williams & Bridges (1964).

In comparison with acetanilide, the additional hydroxyl group that is present in paracetamol would not be expected to induce fluorescence, especially in alkaline solution in which the non-fluorescent phenoxide ion would be present.

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