Biological Half-Life of Psicofuranine in the Human

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On the basis of mean serum psicofuranine levels in the human following oral administration of psicofuranine tetraacetate, a biological half-life of 140 min. has been observed. This is quite similar to the 115 min. reported for the dog, indicating that the marked species difference seen in the gastrointestinal absorption of this nucleoside is not reflected in its biological half-life.

A PRONOUNCED species difference in the oral absorption of psicofuranine (6-amino-9-β-D-psicofuranosyl purine) has been observed. This nucleoside has demonstrated antibacterial activity in mice (1) and antitumor activity in rats (2) on oral administration. Moreover, psicofuranine was shown to be well-absorbed from the gastrointestinal tract of the dog, with a high percentage of an oral dose excreted intact in the urine (3). However, significant oral absorption in the human failed to occur as determined by blood level measurements utilizing microbiological (4) and chemical assays (5). Oral administration of psicofuranine in the form of its lipophilic tetraacetate gave good absorption in the human, with only free psicofuranine detectable in the serum and urine (6). Accordingly, the biological half-life of psicofuranine in the human has been determined following oral administration of the tetraacetate to permit a comparison with results reported for the dog (7).

EXPERIMENTAL

Psicofuranine tetraacetate, 1.5 Gm., was administered orally to each of six adult subjects. Serum samples were collected just prior to drug administration and at 1, 2, 4, 6, and 8 hr. posttreatment. Psicofuranine levels in the serum were determined by the diphenylamine procedure (5). This method does not differentiate psicofuranine from its tetraacetate. However, utilizing microbiological techniques, it was shown earlier (6) that only free psicofuranine is detectable in human serum following oral administration of the ester.

RESULTS

Average serum psicofuranine levels for the six subjects are shown in Fig. 1 (plotted logarithmically). Assuming a pseudo first-order appearance in the serum after a lag time, the data have been fitted by the equation

$$[C, \text{ mcg./ml.}] = 30\,(e^{-0.005t} - e^{-0.015t})$$

where $t = (t_{obs} - 24)$ min.

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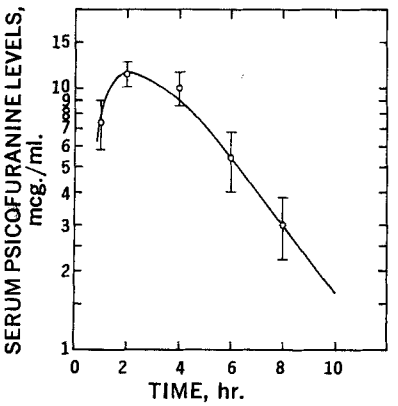

Fig. 1.—Mean serum psicofuranine levels (±s.e.m.) for six subjects receiving 1.5 Gm. of psicofuranine tetraacetate orally.

From this, a half-life of about 45 min. is obtained for the appearance of psicofuranine in the serum, representing the processes of absorption and enzymatic hydrolysis. The biological half-life for drug disappearance is approximately 140 min. and quite similar to the value of 115 min. found in the dog (7). Therefore, the marked species differences between the dog and the human for psicofuranine absorption are not reflected in the biological half-life of this nucleoside. More comprehensive studies of the biopharmaceutics of this interesting agent have been precluded by its serious toxicity (pericarditis) in man at doses required for antibacterial and antitumor chemotherapy (8).

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