

Table 1. CATECHOLASE ACTIVITY AS MEASURED BY THE INCREASE IN EXTINCTION AT 366 m $\mu$ /MIN/MG OF PROTEIN

	Low water table	High water table	
<i>Senecio squalidus</i>	2.400	4.271	Not tolerant of flooding
<i>Senecio jacobea</i>	0.238	0.162	
<i>Senecio viscosus</i>	0.199	0.172	
<i>Hieracium pilosella</i>	0.156	0.086	
<i>Potentilla anserina</i>	0.019	0.006	Tolerant of flooding
<i>Glyceria maxima</i>	0.004	0.011	
<i>Polygonum amphibium</i>	0.004	0.003	
<i>Deschampsia caespitosa</i>	0.002	0.003	
<i>Mentha aquatica</i>	0.001	0.005	

In a cuvette ( $d = 1$  cm) were 1.8 ml. of 0.1 molar tris buffer, pH 8.0; 0.01–0.1 ml. of root extract; 0.1 ml. of 0.1 molar catechol, and the total volume was 3.0 ml.

whether the plants were grown in high or low water table conditions. It is therefore not possible to link the high level of catecholase activity with a premature ageing of the tissues brought about by the adverse water table conditions. Although it is still impossible to conclude anything further about the function of phenol oxidases from these experiments, the clarity of the division in their ecological occurrence may be a useful beginning in understanding their role in plant metabolism. It is known that small concentrations of catechol inhibit oxidative phosphorylation<sup>7</sup> and it could be that phenol oxidases are essential to plants that rely on oxidative phosphorylations, but that they may be dispensed with in those plants that have a predominantly anaerobic habitat for their roots.

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## PSYCHOLOGY

### Time Course of Action of Diazepam

DIAZEPAM ('Valium', Roche) is a recently introduced anti-anxiety drug of the 1,4-benzodiazepine series<sup>1,2</sup>. Clinically, it is usually said to act for 6–8 h, but quantitative data about the time course of functional changes in man do not appear to be available. Measurements of changes in the visual critical flicker fusion threshold (CFFT) and its auditory equivalent, the auditory flutter fusion threshold (AFFT), have been used for this purpose and the results are reported below. The fusion thresholds measure the ability of subjects to discriminate between rapidly repeated sensory stimuli, and both have been shown to be sensitive to the effects of small doses of centrally acting drugs<sup>3–6</sup>, which may impair or improve this discrimination.

The method used to determine the auditory flutter fusion threshold<sup>4,6</sup> essentially involved presenting subjects with interrupted random noise signals (with an on-off ratio of 9:1 and signal intensity of 55 dB re: 0.0002 dynes/cm<sup>2</sup>) and determining the fastest interruption rate at which the interruptions ("flutter") could be clearly and consistently detected. Critical flicker fusion thresholds were similarly determined, using a neon lamp driven by a rectangular pulse generator with an on-off ratio of 1:1, and recording the fastest flicker rate which could be detected. Descending sequences of interruption rates were used in both the flutter and flicker investigations.

Twelve normal subjects (aged 21–30) were given 10 mg diazepam and a placebo on two occasions, 7 days apart, in a double blind cross-over trial. This is a dose which is frequently used in clinical practice. The subjects were allowed a light breakfast and the tablets were taken by mouth 0.5–1 h later. All experiments were started be-

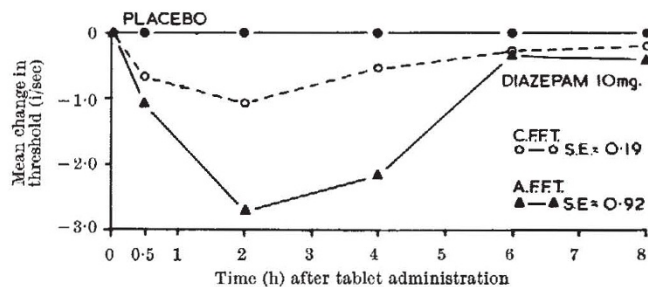


Fig. 1. The time course of the depression of the mean auditory flutter fusion threshold (AFFT, continuous line) and the visual critical flicker fusion threshold (CFFT, broken line) after administration of 10 mg diazepam to twelve subjects. The thresholds recorded with the placebo are represented by the zero baseline. At each time the change in threshold from that recorded before tablet administration is shown.

tween 9 and 9.30 a.m. and thresholds were recorded before administering the tablets and again 0.5, 2, 4, 6 and 8 h later. At each session two AFFT and two CFFT determinations were made. The changes in the mean thresholds at each time compared with the values recorded before tablet administration were subjected to analysis of variance for factorial designs. The results are illustrated for both AFFT (solid line) and CFFT (broken line) in Fig. 1 where the results with the placebo are represented by the baseline.

The pre-treatment mean AFFT was 41.79 interruptions per second (i/sec) and for CFFT 38.11 i/sec on the placebo and 41.00 i/sec (AFFT) and 37.79 i/sec (CFFT) on the active tablet. As is usual<sup>3</sup>, the AFFT rose on the placebo during the day (to 4.80 i/sec more than the starting value by 8 h) whereas the CFFT remained just below the initial level (by -0.60 i/sec at 8 h).

There was statistically significant depression of both AFFT ( $P < 0.05$ ) and CFFT ( $P < 0.001$ ) over the whole period and the time course of the depression was similar for both flicker and flutter fusion. The effect was already present 30 min after administration of the drug and maximal at 2 h. The values then gradually returned to the baseline, the effects having virtually disappeared by 8 h.

Schwartz *et al.*<sup>7</sup> used tritiated diazepam in two human subjects, and showed that the peak blood level was obtained at 2 and 4 h after oral administration. The disappearance of radioactivity from the circulation was in at least two phases, an initial fast component (half life 7 and 10 h) and then a slower phase (half life 2.6 and 2.7 days).

Functional changes rather than chemical changes were measured in the present investigation. Reductions in flutter and flicker fusion thresholds represent impairment of the ability of subjects to discriminate between rapidly repeated sensory stimuli and diazepam in the dose used had this effect. Measurement of the alterations at regular time intervals after administration of such a drug seems to be a highly sensitive technique for determining its time course of action in man.

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