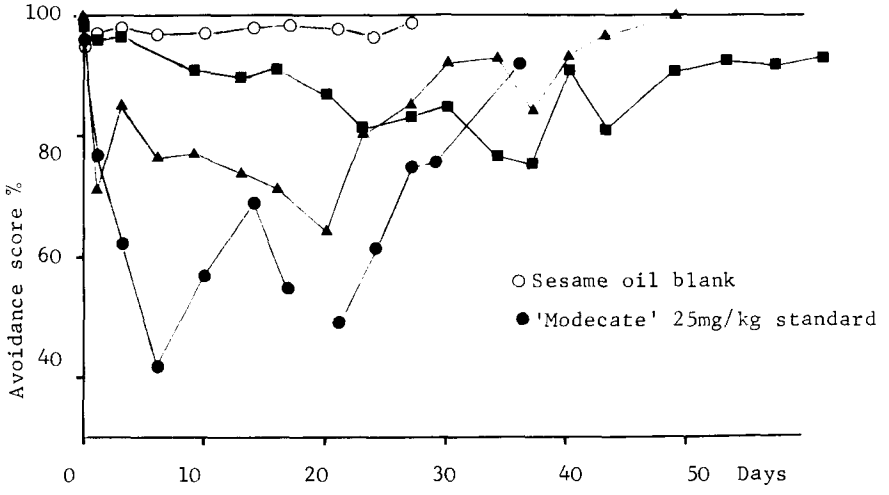
INTRAMUSCULAR FORMULATIONS OF FLUPHENAZINE AND THEIR DURATION OF ACTIVITY IN THE RAT

A.T. Florence, W.R. Vezin, M.L. Ray-Johnson* and H.N.E. Stevens*, Department of Pharmaceutics, University of Strathclyde, Glasgow G1 7XW,
*E.R. Squibb, International Development Laboratory, Moreton, Merseyside

Experimental formulations of psychotropic drugs, particularly fluphenazine, have been prepared in attempts to determine the features of intramuscular formulations which determine the duration of activity, using as standard the currently available long-acting commercial formulations of fluphenazine heptanoate and decanoate in sesame oil, which have durations of activity of 2 - 4 weeks.

The Tenen box for measuring the effect of psychotropic agents, in the rat, by the degree of abolition of conditioned avoidance of 'standard' electric shocks, was used to measure the duration of activity of formulations of fluphenazine and its compounds. In order to average individual differences amongst animals, five animals were used per formulation test. Although the duration of activity is determined by the physico-chemical properties of the drug and the formulation material, and is best monitored in vivo after prior in vitro testing, by analysis of excreted metabolites, the criteria of psychtropic activity are ultimately behavioural, and such methods provide a valuable initial screening procedure for hopeful formulations, prior to the more precise, but expensive and time consuming, excretion analyses.

Formulations studied have been confined to solutions of a range of esters of fluphenazine in gelled and ungelled oils, (triglycerides, long chain mono-functional aliphatic esters and n-paraffins), aqueous suspensions of polymerised fluphenazine esters, solid suspensions of fluphenazine in biodegradable polymers and solidified O/W emulsions of long-chain aliphatic esters of fluphenazine, with a range of particle sizes. Of these methods, formulations in oils, though being used at present for commercial long acting preparations, appear to be the least promising means of further extending duration of activity.



Psychotropic abolition of respondent conditioning fluphenazine azelaate 5% w/v in 6:4 Arachis oil 50 mg/kg, (■) and fluphenazine octadecanoate, 20% aqueous suspension, 10-20 µm, 50 mg/kg (▲)

Tenen, S.S. (1966). Psychonomic Science, 6 (9), 407 - 8.

We thank E.R. Squibb for support of W.R.V.