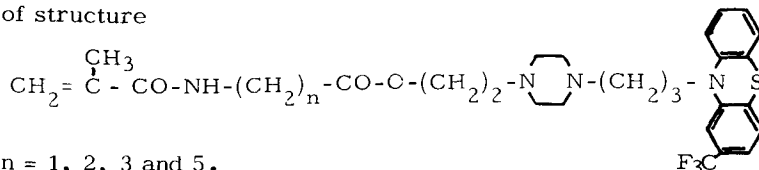


BIOLOGICALLY ACTIVE POLY(N-METHACRYLOYL ω -AMINO ACID) ESTERS OF FLUPHENAZINE AND THEIR DURATION OF ACTIVITY

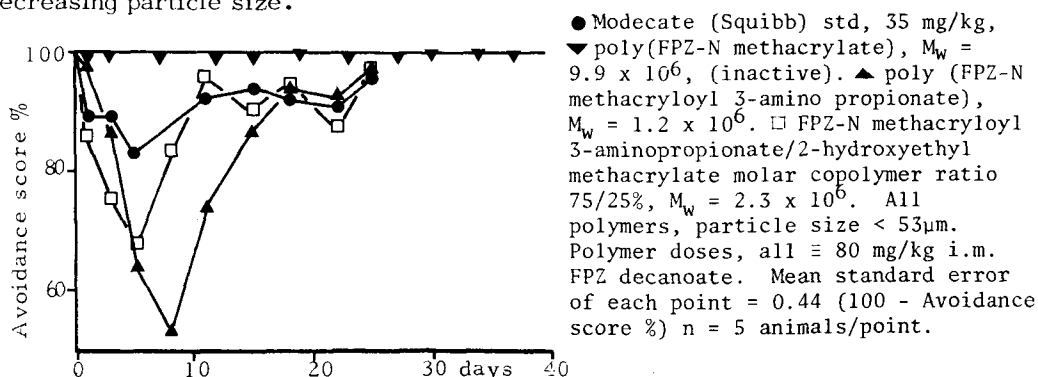
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Fluphenazine esters are pro-drugs from which active drug is formed *in vivo* over a period of weeks when administered as oily solutions. Polymeric esters of drugs can be formed which have the potential to act as their own depot. With polymers there is scope for altering the molecular parameters to alter disposition and duration of drug activity. We have prepared monomeric esters of fluphenazine (FPZ) of structure



where $n = 1, 2, 3$ and 5 .

These have been synthesized by condensation of the N-methacryloyl amino acid (Batz & Koldehoff, 1976) with FPZ, using dicyclohexylcarbodiimide. It is possible to obtain nearly quantitative yields of crude monomer, which may be purified by crystallisation of dimaleate salts from polar organic solvents. Homopolymers, and copolymers with hydrophilic methacrylates such as methacrylic acid and 2-hydroxyethyl methacrylate have been prepared by bulk and solution polymerisation and tested at equivalent dosage and particle size by a rat conditioning test previously used for formulations of FPZ (Vezin & Florence, 1978). Some results are shown in Fig. 1. Molecular weights were determined by light scattering. Polymers with drug attached directly to the backbone (e.g. fluphenazine methacrylate) are not biodegradable and thus are biologically inactive, but we have observed that homopolymers of I are slowly biodegradable when $n = 2$ or 3 , but nearly inactive when $n = 5$; degradability is not enhanced by copolymerisation with small molar ratios ($\sim 20\%$) of methacrylic acid as Harris and others (1976) found with polymerised herbicides. We have observed that degradability increases with decreasing particle size.



We thank the Scottish Home and Health Department for financial support.

Batz, H.G. Koldehoff, J. (1976) Die Makromolekulare Chemie, 177: 683-689.
 Harris, F.W., Aulabaugh, A.E. and others in Faul, D.R., Harris, F.W. (Eds.) Controlled release polymeric formulations, ACS Symposium series, 33: 222-230
 Vezin, W.R., Florence, A.T. (1978) J. Pharm. Pharmac. 30: 28