AMITRIPTYLINE-EUDRAGIT L COMPLEX AS A SUSTAINED RELEASE PREPARATION

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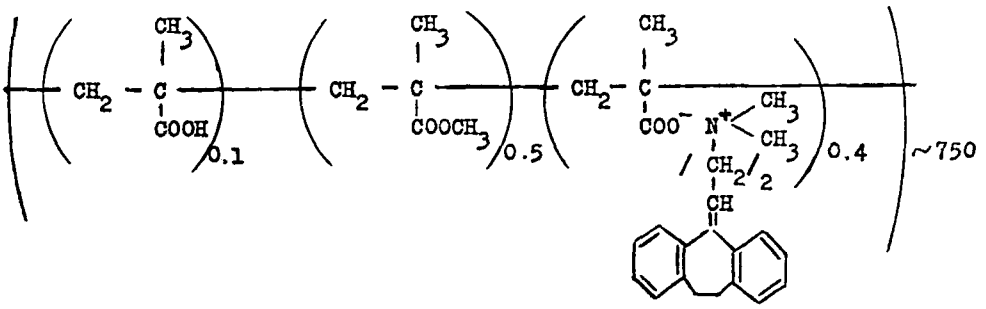
Eudragit L, a methacrylic acid-methacrylic acid methyl ester (1:1) copolymer, forms water-insoluble complexes with some drugs containing amino or imino groups. In the gastrointestinal tract the drugs are released from these complexes slowly by ion exchange processes (Orban et al 1981).

An amitriptyline-Eudragit L complex was prepared by reaction of an aqueous solution of the sodium salt of Eudragit L with an aqueous solution of amitriptyline HCl. Only 80% of the carboxylic groups of the Eudragit L could be utilized for complex formation. The chemical structure of the complex confirmed by i.r. spectroscopy, is :



In vitro about 60% of the drug was released from the complex agitated in simulated gastric fluid at 37°C for 1h, while the amitriptyline HCl powder dissolved completely in 5 min under the same conditions.

The in vivo absorption of the drug was compared in dogs given 15 mg kg^{-1} [^{14}C]amitriptyline base (79.9μCi kg^{-1}) as the hydrochloric acid salt or in the form of the Eudragit L complex of amitriptyline. The areas under the serum concentration curves showed that in the first 2h after administration 2.5 times more drug was absorbed from the salt form than from the complex form, but there were no significant differences between the two forms according to the absorbed quantity of drug over 0 - 12h, and the excreted radioactivity into the urine over 0 - 72h.

Absorption in man was studied on six healthy volunteers given 50 mg amitriptyline base as the hydrochloric acid salt (in a quick release coated tablet) or in the form of Eudragit L complex (as a hard gelatin capsule). Comparison of the areas under the serum concentration curves showed that in the first 4h after administration only half as much drug was absorbed from the complex form as from the salt form, but after 24h the absorbed quantity of amitriptyline from the two dosage forms was almost the same.

Therefore the amitriptyline-Eudragit L complex seems to be useful for sustained release medication of amitriptyline.

Orban et al 1981, B.P. 1.596.166 (18 Nov.)

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