IPORSIP'98

POSTER PRESENTATIONS
FRIDAY, JULY 24, 1998
CADD SESSION

QSAR-Study On A Series of 2,4-Disubstituted Thiazoles With Anti-inflammatory Activity

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The chemical structure of newly synthesized Thiazoles is described by lipophilicity parameter CLOGP, polarisability parameters, electronic MO parameters and steric parameters. The anti-inflammatory activity is presented as log%, where % is the percentage of decreasing edema, evaluated using the carragenin induced edema test in vivo on mice ACR. The results from the QSAR study indicate that a nonlinear relationship between biological activity and lipophilicity of the compounds exists with optimum logP 1.96. Also, the QSAR-Studies shows that the electrostatic interactions between the compounds and their binding sites are of importance. Thus, wide negative parts of the VdW surface area increase the biological acivity: On the basis of these results is design and synthesized a thiazole derivative C5. It manifests the highest biological activity for the series investigated. This compound will be objective for further pharmacological and toxicological tests as a potential anti-inflammatory drug.

Drug Release From Polydisperse Pellet Preparations-Computer Simulations And Kinetic Analysis

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Each dose of a pellet preparation consists out of dozens of single drug carriers. The methods to analyze the release kinetics of drug from multiunit pellet systems which are published in the literature until now, describe the total release kinetics of these complex systems phenomenologically using simple mathematical equations. In the present investigations a new mathematical model has been developed which takes into account that the release profiles of drugs from polydisperse multiunit preparations like diffusion pellets represent the sum of the individual release curves of the single pellets. The results of the investigations show that only in homogeneously coated monodisperse pellet systems the total release reflects the release of the single drug carriers. In polydisperse particulate systems there are particles with different particle sizes. The particles are different in weight and surface area. The relation between weight and surface area is particle size dependent, too. The total release curves of polydisperse pellet preparations reflect the particle size distributions. Computer simulations were carried out to characterize the release patterns of hypothetic pellet preparations. The size dependent theoretical release patterns of drugs with high, medium and low solubility in an aqueous medium were calculated. The release from single pellets and from batches with different particle size distributions were calculated. The results show a zero order release from each single pellet of a polydisperse system will not result in a zero order kinetic of the preparation. The result of the investigations show that curve fitting procedures using the total release curve of polydisperse pellet preparations will give only very limited information about the characterized system and will give no insight into the release processes.