IPORSIP '98

POSTER PRESENTATIONS
SATURDAY, JULY 25, 1998
CADD SESSION

Map-Based Structure- Anticonvulsant Activity Study of Some Valproic Acid Derivatives

T. Netzeva, R. Natcheva, I. Doytchinova
Department of Chemistry, Faculty of Pharmacy, Medical University, 2 Dunav str., Sofia 1000, Bulgaria

Valproic acid (VPA) is the most important and widely used anticonvulsant drug. Now, the search for a new, highly active and less toxic VPA derivatives is in progress.

The aim of this study is to investigate the role and the significance of the steric and electrostatic features of 32 molecules-VPA metabolites and analogues, for the rise and strength of their anticonvulsant activity.

Molecular geometry of all compounds is optimized by the semiempirical molecular orbital AM1 method. The Van der Vaals'volume and electrostatic potential maps are calculated and visualized using Chem-X computer program.

It was found that for the compounds with saturated hydrocarbon chains the shape and size of the molecules are important. For unsaturated compounds and those containing an additional oxygen atom (as –OH or =O) in different position according to the –COOH group, the number and localization of the negative potential regions are of great significance.

In conclusion, it is reasonable to assume that anywhere in the mechanism of indirect increasing of GABA levels, a specific ligand-receptor or ligand – enzyme interaction of VPA and its derivatives exist.

Computer-Aided Study On Complexation of Coumarine Derivatives With Lanthanides- Cytotoxic Profiles of The Complexes

I. Kostova[1], I. Manolov[2], S. Konstantinov[3], T. Netzeva[1], M.H. Karaivanova[3]
[1]Department of Chemistry, [2]Department of Industrial Pharmacy, [3]Department of Pharmacology and Toxicology, Faculty of Pharmacy, Medical University, 2 Dunav Str., Sofia 1000, Bulgaria

The complexes of types $Ln(HW)_3.nH_2O$ and $Ln(HC)_3.nH_2O$ [where Ln = Ce, La, Nd; HW = Warfarin; HC = Coumachlor) have been synthesized by interaction of Warfarin sodium, resp. Coumachlor Sodium and the appropriate lanthanide nitrates in various stoichiometric ratios. The structures of the solid complexes have been characterized and identified on the basis of elemental analysis, conductivities, IR-spectroscopy and ^{1}H-NMR-spectroscopy.

The partial charges and nucleophilic superdelocalisabilities of heteroatoms in ligands molecules are calculated using semiempirical quantum mechanical method AM1.

It is supposed that the lacton- and the keto-carbonyl groups of the ligands are bonded to the metal ion as bidentate ligand. The theoretical data are in a good agreement with the results from the spectrophotometric analysis. The conductivity measurements show non-electrolytic nature of the complexes.

Cytotoxicity determination by MTT-assay showed that the inorganic salts and the complexes with Warfarin did not have any significant activity. The complexes with Coumachlor were found to be more cyctotoxic. The most active compound was the complex of Cerium with Coumachlor. All tested complexes showed similar in vitro cytotoxic profiles. This fact is in agreement with the proposed chemical structures.