Description of physicochemical properties of acyclovir derivatives and their cyclodextrin complexes

Summary

The discovery of acyclovir (ACV), the first potent and selective antiviral drug, has stimulated the synthesis of its analogues. The modification of the acyclic side chain creates several new compounds of significant antiviral activity e.g. gancyclovir or pencyclovir. The next step was the modification of the guanine moiety of acyclovir which resulted in the formation of several compounds with appreciable antiviral activity.

The tricyclic analogs of ACV and their inclusion complexes with cyclodextrins are subjects of my research. The analogs of ACV obtained by modification of their guanine moiety were synthesized by Prof. B. Golankiewicz and co-workers in Institute of Bioorganic Chemistry PAN. Tricyclic acyclovir derivatives have different physicochemical properties, but their biological activity although changed, is still present.

The aim of my doctoral thesis is to determine physicochemical properties of studied compounds and their cyclodextrin complexes by the use of the solubility method, solvent – solvent extraction experiments and thermal analysis method. Solubility in water and 1–octanol (at different temperatures and pH values of solution), partition coefficient between water and organic phase, melting temperatures and molar enthalpies of fusion have been determined for all the investigated substances. To study the stability, structures and thermal characterization of inclusion complexes between tricyclic acyclovir derivatives and chosen cyclodextrins the Higuchi-Connors solubility method, ¹H NMR, differential scanning calorimetry (DSC) measurements and molecular modeling calculations have been used. Results of these experiments enabled me to confirm inclusion complex formation, to determine their stability constants and to calculate optimizing structure of those complexes.

The doctoral thesis consists of the description of measurements, apparatus used, experimental data and calculated results. The literature data containing antiviral drug structures and physicochemical properties, cyclodextrin complexes with antiviral drugs and methods used in cyclodextrin inclusion complexes study were also included to this thesis. At the end of the thesis there are certain conclusions proving that the usage of cyclodextrin changes positively properties of the studied compounds, e.g. enhances their solubility in aqueous solutions.