Abstract

The aim of this thesis is to study the formation of inclusion complexes of acridonic and acridinic sulfonamides, recently introduced into the pharmaceutical drugs area, and not studied until now from this point of view. These complexes are also, of biopharmaceutical importance, as new forms of molecular capsulation.

The studies are based on a comprehensive and critical analyse of the literature referring to sulfonamides, to their place and particularities in the system of pharmaceutics, and to the “host” molecules, especially cyclodextrines, as well as to the most adequate modern methods, in their research.

The results obtained have exceeded our initial expectations. Numerous aspects that were outlined during the experiments could be understood and explained only after a complex and simultaneous interpretation of all the phenomena and data collected. The chromatographic method (HPLC) has shown that sulfonamides (even though were used substances of at least 99% purity) did not behaved as monocomponents. In our opinion, this contradiction is apparent, and it can be explained with the partial hydrolysis of the amidic bond from the “guest” molecules. This conclusion is also corroborated by some data from the special
literature referring to other sulfonamides, as well as by the fact that the chromatograms of N-acetilated acridonic sulfonamides have an increased number of peaks, due to the presence of two groups, which can hydrolyse with different rates. It is possible that the formation of the inclusion complex formed will catalyse this reaction, a phenomenon also known at some aromatic esters. The formation of the inclusion complexes, even in these special conditions, was investigated by FTIR spectrometric method, and comparing the spectra of both each pure substances and their complexes - we have drawn the conclusion that in this particular case of the studied systems – the complexes - are not necessarily of ‘inclusion’ character, but they also can be formed on the external surface of cyclodextrines.

One major objective of the study was the calculation of the stability constants of the complexes. In principle, the analyse of the UV/VIS spectrophotometric method using the Benesi-Hildebrand’s equations, later modified by Scott, permits these determinations for complexes of 1:1 type, for which the proposed equation is linear. Measuring the absorbencies in function of time, we observed that at an early stage linearity is kept, but in time more and more aberrations appear, especially in the presence of cyclodextrins. This fact confirms our hypothesis - deduced from the HPLC measurements- regarding to the partial hydrolysis of sulfonamides. For calculation of the stability constants we proposed a modification of the Benesi-Hildebrand-Scott’s equation.

The conclusions deduced from the results of the chromatographic and spectrometric experiments were compared and completed with the modeling of the complexes using the Chembio 3D program, version 11.0.