Abstract

Spectral and chromatographic investigations of forty biologically active ampholytic substances exhibiting, in majority of cases, therapeutic activity enabled determination of nine spectral characteristics and retention parameters of the compounds referring to their separation on three polar and six nonpolar and semipolar HPLC columns at three pH regimes of water phase. Applying quantum chemistry and based on additivity rules methods, numerical values of twenty-nine descriptors reflecting various physicochemical features of the compounds were determinated. To consider correlations between: biological properties/therapeutic activity, spectral properties and behaviour of the compounds upon HPLC analyses, and physicochemical descriptors, the following chemometric tools were used: Principal Component Analysis (*PCA*), Genetic Algorithm together with Partial Least Squares (*GA–PLS*) method, Genetic Algorithm together with Multiple Linear Regression (*GA–MLR*) method and Supported Vector Machine (*SVM*) classification approach together with linear decision surface algorithm. The undertaken investigations revealed that differentiation of the compounds in context of their specific biological activity/therapeutic relevance is possible. In particular, it was found that values of linear analytical function determined by nineteen descriptors reflecting bulkiness, electronic and spectral features of molecules are positive for compounds acting on the central nervous system and negative in the case of substances acting on pathogenic microorganisms. The classification model found permits differentiation of ampholytic substances in context of: their biological/therapeutic features, prediction of these features in the cause of untested chemicals, as well as design of therapeutic agents. Three linear equations relating logarithms of values of energy of long wavelength absorption bands with values of physicochemical descriptors referring to bulkiness, electrophilic or nucleophilic features of ampholytic substances can be a useful tool for predicting spectra characteristics of untested compounds. Similarly, obtained – applying *GA–MLR* approach – linear equations (in number of six) relating logarithms of values of retention coefficients (log k_w) with values of physicochemical parameters determined computationally or experimentally form a useful framework to: model conditions of chromatographic analyses and separations, predict retention parameters/*n*-octanol/water partition coefficients (reflecting lipophilic/hydrophobic features) of untested compounds, and gain therapeutically interesting information on biologically active substances which are structurally and behaviorally related to the compounds investigated. Analysis of influence of descriptors appearing in the analytical equations on values of log k_w enables evaluation of

behaviour of the compounds investigated in biological environment, also in various parts of man alimentary canal. The use of chemometric methods revealed that modeling of biological/therapeutic features of ampholytic compounds is possible without necessity of carrying out time-consuming and expensive laboratory tests.