THE REACTIVITY OF N-[(2-OXOINDOLIN-3-YLIDENE)-2- OXIACETYL] AMINO ACIDS

Popov Yu., Kolisnyk S.V., Sviechnikova O.M.*, Sipliva I.V.
The National University of Pharmacy, Kharkiv, Ukraine
*H.S. Skovoroda Kharkiv National Pedagogical University, Kharkiv, Ukraine
vph_secretary@mail.ru

N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl] amino acids and their derivatives possess various types of biological activity, that is why, this class of compounds is intensively used for purposeful search of active pharmacophores. Pharmacological activity depends on the pharmacophore capacity of forming complexes with biological receptors which, in turn, is determined by the pharmacophore reactive ability, particularly, its acid-base properties. Therefore, the investigation of reactive power of the biologically active substances homological series represents undoubting scientific and practical interests which are connected with the strong possibility of optimization of these xenobiotics artificial synthesis and their active pharmacophore abilities modeling improvement.

The compounds ionization constants were determined by potentiometric titration method. The titrant was 0.05 M potassium hydroxide aqueous solution which did not contained CO_2. The concentration of the titrated solutions was 0.005 M at the point of neutralization. The measurements were performed by EV-74 ionomer with the usage of two electrodes: a glass (ESP 43-074) indicatory one as well as a saturated chlorine-silver one. The latter was applied as a comparison electrode. The determinations were carried out at 25^0C in triplicates. The precision of the obtained results was evaluated by small selections mathematic statistics method (confidence probability - 0.95). The mixed solvent dioxane - water (60 volume % of dioxane) was prepared of freshly bi-distilled water free from CO_2 and of 1,4-dioxane (very pure) which did not undergo an extra purification.

The experimental compounds were proven to be weak dibasic acids. Their pKa magnitudes were determined by Noyers method. The correlation of these magnitudes to both of the reactive sites (COOH- and OH-groups) was performed. Each CH_2-prolongation step of the polymethylene chain length was shown to weaken acidity at both reactive sites ionization. Hammett correlation equations ($pKa_{1,2} - f(\sigma)$) were calculated for N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl] amino acids which allows to predict acid-base properties of these homological series compounds. Low susceptibility of the reactive sites towards polymethylene chain prolongation was established. The obtained results are being used to QSAR-analyze the compounds of these iso-structural series by mathematical modeling.