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The service of *in silico* methods in the development of metabolically stable ligands

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Various *in silico* methods have become an integral part of the modern process of drug design and development. Their service is not only limited to the selection of compounds with potential activity towards particular target, but they also enable the initial evaluation of the physicochemical and pharmacokinetic properties of compounds [1,2].
Within the study, a series of derivatives of the selective agonist of serotonin receptor 5-HT_7, LP-211, were synthesized. The compounds were examined in terms of their activity towards 5-HT_7R, but also their metabolic stability properties were assessed. The promising properties of one of the compounds, determined its selection for further *in vivo* studies.
In order to support the design of new stable 5-HT_7R ligands, a protocol for *in silico* evaluation of metabolic stability was developed. It involved the description of compounds with the use of a hybrid representation of various one-, two- and three-dimensional descriptors generated in the PaDEL-Descriptor [3] and application of the machine learning algorithm – Support Vector Machine adjusted for performing regression tasks [4]. The obtained results were compared with the outcome of the set of online tools allowing for direct or indirect evaluation of compound's metabolic stability properties.

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