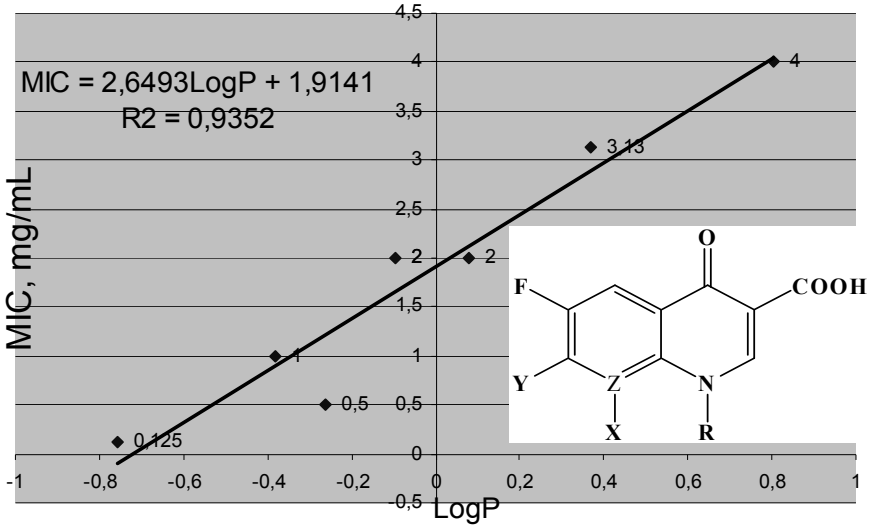
INVESTIGATION OF THE QUANTITATIVE RELATIONSHIP BETWEEN STRUCTURES – ANTITUBERCULAR ACTIVITY FLUOROHINOLONES DERIVATIVES WITH SETTLEMENT PLATFORM MOLINSPIRATION CHEMINFORMATICS

Serdyuk A.A., Redkin R.G. Shemchuk L.A., Chernykh, V.P.
The National University of Pharmacy, Kharkiv, Ukraine
nastya.serdyuk.96@mail.ru

In Ukraine, the epidemic of tuberculosis (TB) has passed into the category of national problems, as has become difficult to manage as the number of TB patients has exceeded 1% of the population. Every year the number of patients increased by 40 thousand people and 10 thousand people die annually. In the World, there are approximately one third of populations infected with TB bacillus and 1.7 million people die from TB annually, and new TB patient is estimated at 8 million or more. TB has been consequently identified by the WHO as one of the three priority diseases for drug research and development. Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) make this problem become more complex. Importantly, the WHO also recommended the use of fluoroquinolones (FQ) – Levofloxacin or Moxifloxacin for the treatment of XDR-TB.



We investigated the quantitative relationship between the molecular structure of FQ and their anti-TB activity using the method of cheminformatics – settlement platform Molinspiration Cheminformatics (University of Bratislava, Slovakia). To do this, we have considered such settlement quantum chemical descriptors as octanol-water partition coefficient (LogP), topological polar surface area (TPSA), molecular volume (MV, expressed in cubic Angstroems (Å3). For the study we selected 11 FQ with known quantities the minimum inhibitory concentration (MIC, μg/mL) – Ciprofloxacin, Ofloxacin, Pefloxacin, Enoxacin, Levofloxacin, Sparfloxacin, Temafloxacin, Moxifloxacin, Grepafloxacin, Trovafloxacin, Gemifloxacin. As a result, we obtain three equations correlation of MIC values LogP, TPSA, MV. The highest level of reliability (coefficient approximation - R2) was found for the dependence of MIC & LogP (R2 = 0.9352, N = 7) for MIC&MV (R2 = 0.9148, N = 6), and the lowest for MIC&TPSA (R2 = 0.8741, N = 5). The proposed algorithm can be used to determine and describe the quantitative relationship between anti-TB activity and chemical structure in a series of fluoroquinolones in order to synthesis and search for new anti-TB drugs.