

ACRAB-TOLC EFFLUX PUMP INHIBITOR ANALOG SYNTHESIS

ACRAB-TOLC EFLUKSA SŪKŅA INHIBITORA ANALOGU SINTĒZE

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Bacterial resistance to the existing classes of antibiotics is one of the most important challenges for the future healthcare system and bacterial cells efflux pumps play an important role for this internal drug resistance. To reduce the ability of the efflux pumps binding to medication substrates, the molecules called efflux pump inhibitors are used to rejuvenate the antibiotics activity by binding to the efflux pump protein [1].

In the framework of the project, it was hypothesized that AcrAB-TolC efflux pump outer membrane protein TolC in Gram-negative *E.coli* bacteria cells could represent an attractive drug target. Therefore, structure analogs of known clinical candidate compound have been synthesized and identified their structure-activity relationships (SAR) to TolC efflux pump [2].

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References:

- [1] AlMatar. M., Albarri. O., Makky. E. A., Köksa. F. *Pharmacol Rep.*, **2021**, 73, 1-16.
- [2] Ott. G. R., Cheng. M., Learn. K. S., Wagner. J., Gingrich. D. E., Lisko. J. G., Dorsey. B. D. *Journal of Medicinal Chemistry*, **2016**, 59(16), 7478-7496.