

MEETING ABSTRACTS

FACILE SYNTHESIS OF CYSTEINE-ACETYLCHOLINESTERASE TARGETED INSECTICIDES

Miroslav Psotka^{1,3}, Lukas Gorecki^{1,2}, Barbora Svobodova^{1,2}, Kamil Musilek^{1,3}, Daniel Jun^{1,2}, Jan Korabecny^{1,2} and Kamil Kuca^{1,3}

¹ University Hospital Hradec Kralove, Biomedical Research Centre, Sokolska 581, 500 05 Hradec Kralove, Czech Republic; miroslav.psotka@gmail.com;

² University of Defence, Faculty of Military Health Science, Department of Toxicology and Military Pharmacy, Trebesska 1575, 500 01 Hradec Kralove, Czech Republic;

³ University of Hradec Kralove, Faculty of Science, Department of Chemistry, Rokitanskeho 62, 500 03 Hradec Kralove, Czech Republic

Malaria is annually responsible for more than 400 thousands casualties. The disease is transmitted via infected female *Anopheles* mosquitoes. Spread of the malaria can be prevented by using either chemical compounds known as insecticides or by genetically engineered plants.^[1,2] Mechanism of action of currently deployed insecticide involves inactivating acetylcholinesterase (AChE, EC 3.1.1.7) enzyme by binding to Ser360 (*Anopheles gambiae* numbering). More recently, Cys447 located close to active site entrance was emerged as an alternative target to overcome insecticide resistance and also improving selectivity towards insect AChE over mammalian one.^[3] In our contribution, we have developed novel, straightforward and facile synthesis for Cys-targeted insecticides containing either maleimide or succinimide scaffolds. Employment of Grubbs olefin metathesis allowed us to obtain the final compounds in multistep synthesis in relatively high yields. We propose that the described synthetic route might be used in large scale-up for further studies.

Acknowledgement

This work was supported by Ministry of Health of the Czech Republic (no. 16-34390A) and University of Defence (Long-term organization development plan Medical Aspect of Weapons of Mass Destruction).

References

1. C. M. Fox, K.-S. Kim, P. B. Cregan, C. B. Hill, G. L. Hartman and B. W. Diers, TAG Theor. Appl. Genet. Theor. Angew. Genet., 2014, 127, 43–50.
2. Y. P. Pang, Adv. Insect Physiol., 2014, 46, 435–494.
3. Y.-P. Pang, S. Brimijoin, D. W. Ragsdale, K. Y. Zhu and R. Suranyi, Curr. Drug Targets, 2012, 13, 471–482.