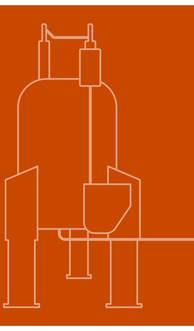
The adipokinetic hormones and their cognate receptor from the desert locust, *Schistocerca gregaria*: solution structure of endogenous peptides and models of their binding to the receptor

BACKGROUND

Neuropeptides exert their activity through binding to G-protein coupled receptors (GPCRs). **GPCRs** are well-known drug targets in the pharmaceutical industry and **are currently discussed as targets to control pest insects**. Here we investigate the neuropeptide adipokinetic hormone (AKH) system of the desert locust *Schistocerca gregaria*.

The desert locust is known for its high reproduction, and for forming devastating swarms consisting of billions of individual insects. It is also known that *S. gregaria* produces three different AKHs as ligands but has only one AKH receptor. The AKH system is known to be essential for metabolic regulation, which is necessary for reproduction and flight activity.

METHODS



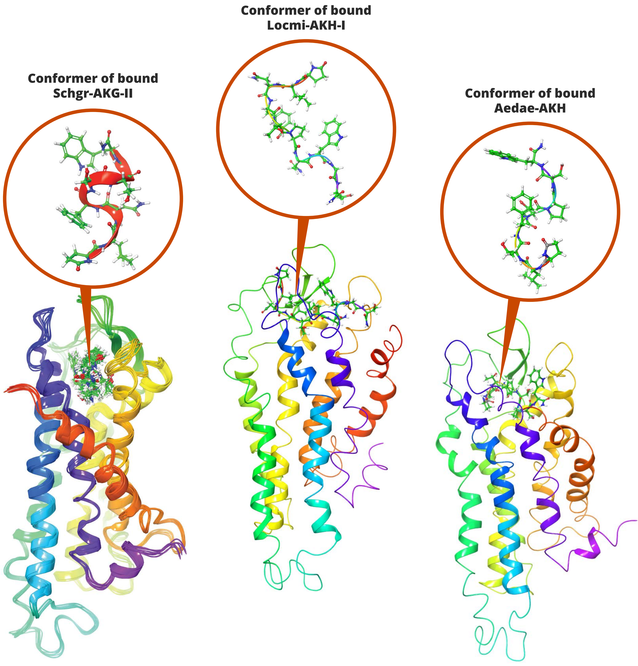
Nuclear magnetic resonance techniques (NMR) in a dodecylphosphocholin (DPC) micelle solution were used to determine the structure of the three AKHs. The primary sequence of the *S. gregaria* AKH receptor (AKHR) was used to construct a 3D molecular model. Next, the 3 AKHs were individually docked to the receptor, and dynamic simulation of the whole ligand-receptor complex in a model membrane was performed.

RESULTS

Although the three endogenous AKHs of *S. gregaria* have quite different amino acids sequences and chain length, **NMR experiments assigned a turn structure in DPC micelle solution for all**. The GPCR-ModSim program identified human kappa opioid receptor (hk-OR) to be the best template after which the *S. gregaria* AKHR was modeled.

All three AKHs were found to have the same binding site on this receptor, interact with similar residues of the receptor and have comparable binding constants. Molecular switches were also identified; the movement of the receptor could be visually shown when ligands (AKHs) were docked and the receptor was activated.

SCHGR-AKHR WITH 3 AKHS IN BINDING POCKET



CONCLUSION

The study proposes a model of binding of the three endogenous ligands to the one existing AKH receptor in the desert locust and paves the way to use such a model for the design of peptide analogs and finally, peptide mimetics, in the search for **novel species-specific insecticides based on receptor-ligand interaction**.

PeerJ

The adipokinetic hormones and their cognate receptor from the desert locust, Schistocerca gregaria: solution structure of endogenous peptides and models of their binding to the receptor.
PeerJ 4:e7541 DOI: 10.7717/peerj.7541
http://peerj.com/articles/7541

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