

Molecular effectiveness of peptides from African medicinal plants decoded

November 22 2013



Peptides are autologous substances that are formed from amino acids, are able to trigger specific reactions in the human body and can influence a variety of physical functions. Cyclical plant peptides, known as cyclotides, have also an effect on the human body. "Until now, however, it has not been fully understood whether these peptides work and on what receptors, nor what form their molecular signalling pathway takes," says Christian Gruber from the Centre for Physiology and Pharmacology at the MedUni Vienna. The molecular effect of peptides from an African medicinal plant has now been decoded for the first time.

The scientists in Vienna have, in collaboration with an international team from Australia, England, Ireland, Sweden and the USA, described a peptide in a plant from the coffee plant family that is similar to the human neuropeptide hormone oxytocin, and which binds to its receptors. This may in the future lead to the development of new medicines.

Cyclotides were originally discovered as ingredients of herbal medicines that are used in the traditional medicine practiced by people from African nations to induce birth and avoid complications afterwards. The plants are prepared as tea ("kalata-kalata") and drunk in order to make the birthing process easier and faster. "Until now, however, we did not know whether there was a specific receptor for these [peptides](#) that caused the uterus to contract," explains Gruber. "We've now found a peptide, Kalata B7, that can not only cause isolated uterine [muscle cells](#) to contract, but also binds to two receptors – the oxytocin and vasopressin-1a receptors – and controls their function."

Using state-of-the-art analytical methods, it has been possible to demonstrate that the plant peptides have a similar structure to human oxytocin. Oxytocin is known as the "happiness hormone" – it is not only important during the birthing process, but also influences the bond between the mother and child as well as interhuman relationships in general.

The study has now been published in *PNAS* and edited by the 2012 Nobel Prize Winner for Chemistry, the American pharmacologist Robert Lefkowitz from Duke University in Durham.

Creation of a "peptide library" for the development of medicines

Says Gruber: "This represents a very important step: We've been able to

demonstrate the mechanism for a specific peptide in this single plant. With this natural blueprint, we have been able to create synthetic ligands that demonstrate better pharmacological properties." Ligands are materials that bind to a receptor and are able to exert an influence on the cell. Adrenaline is a natural ligand, for example, for beta receptors on cardiac muscle cells.

"We now know that these cyclical peptides have an enormous variety of [amino acids](#) and occur in vast parts of the plant kingdom. They have been found in violet, pumpkin and nightshade plants, in legumes and even in certain types of grain. With these results, we are now able to isolate cyclotides from a variety of other [plants](#) and test this library of peptides on various receptors," explains the MedUni Vienna researcher. The aim is to use these latest chemico-biological findings to create ligands for peptide [receptors](#) and turn them into medicines.

More information: Oxytocic plant cyclotides as templates for peptide G protein-coupled receptor ligand design." J. Koehbach, M. O'Brien, M. Muttenthaler, M. Miazzi, M. Akcan, A. Elliott, N. Daly, P. Harvey, S. Arrowsmith, S. Gunasekera, T. Smith, S. Wray, U. Göransson, P. Dawson, D. Craik, M. Freissmuth, C. Gruber., (2013) *Proceedings of the National Academy of Sciences*, [DOI: 10.1073/pnas.1311183110](https://doi.org/10.1073/pnas.1311183110)

Provided by Medical University of Vienna

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