Miniaturized peptide toxins in drug discovery: pro & con's

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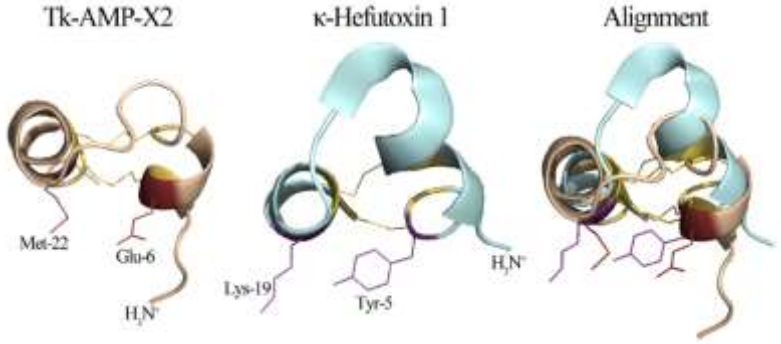
Since the introduction of insulin exactly a century ago, tens of peptide drugs have reached the market for the treatment of a wide range of diseases, from diabetes, cancer, osteoporosis, multiple sclerosis to pain. The often remarkable potency and selectivity of peptides can be seen as a clear advantage in drug discovery. However, there are also limitations in terms of low oral bioavailability and poor plasma stability. Additionally, for many years large-scale synthetic peptide manufacturing was considered exorbitantly expensive, in particular for longer peptides with multiple disulfide bridges. This resulted in a stagnation of peptide drug development. Despite this and thanks to the advent of recombinant technology, we have now arrived in an era where rational design strategies applied to peptides found in nature, from animals and plants, help us to make good progress. To illustrate this, we will present structure-function data of several peptides derived from the venoms of snails, spiders, scorpions, wasps and also from wheat. The interesting structural similarity, for instance, between a defense peptide from wheat (Tk-AMP-X2) and a neurotoxic peptide from scorpion venom (κ-Hefutoxin 1), indeed now permits rational and functional drug design that may lead to antimicrobial peptides.



Examples of miniaturized peptides, while maintaining their pharmacophore and activity, will also be discussed in the light of the evolution of the appearance of their natural precursor peptides.

References:
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