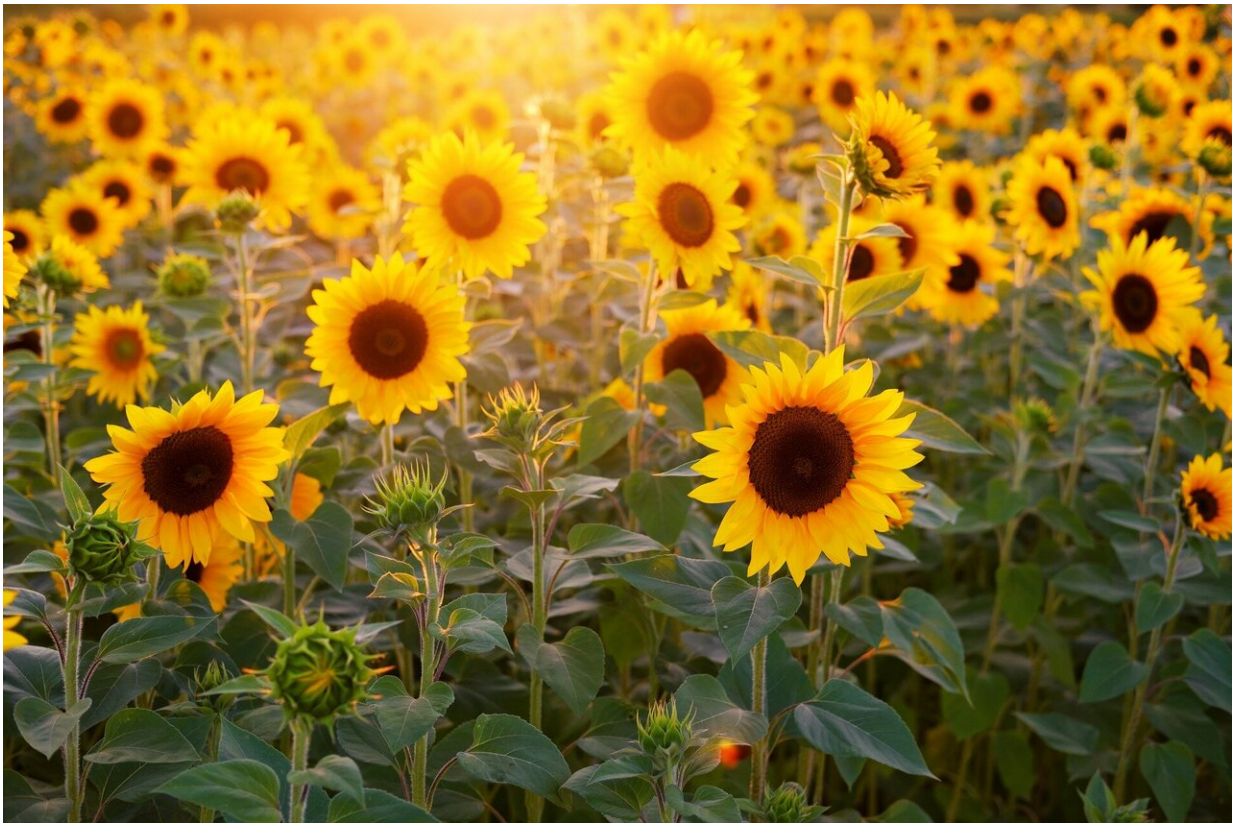


Sunflower peptide as template for potential analgesic

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A naturally occurring peptide in sunflower seeds was synthetically optimized and has now been identified as a potential drug for treating abdominal pain or inflammation (in the gastrointestinal tract, abdominal

area and/or internal organs). That is the finding of an international study led by Christian Gruber from MedUni Vienna's Institute of Pharmacology (Center for Physiology and Pharmacology), which was conducted jointly with the University of Queensland and Flinders University in Australia and has now been published.

The scientific aim of the study is to find analgesics that are only active in the periphery and do not cross the [blood-brain barrier](#), as an alternative to commonly used synthetic opioids. Gruber explains the background: "Morphine was one of the first plant-based medicines and was isolated from the dried latex of poppies more than 200 years ago. It binds to opioid receptors in the brain and is still regarded as the main pillar of [pain](#) therapy. However, there is a high risk of opioid addiction, and an overdose—as a result of this strong dependency—inhibits the breathing center in the brain, which can result in respiratory depression and, in the worst case, in death." For this reason, researchers throughout the world are trying to make analgesics safer and to find active [drug](#) molecules that do not have the typical opioid side-effects.

Sunflower extracts were to some extent used in traditional medicine for their anti-inflammatory and analgesic properties. In the current study, the scientists from Austria and Australia, primarily Ph.D. student Edin Muratspahić, isolated the plant molecule that may be responsible for this effect. Medicinal chemistry methods were then used to optimize the so-called sunflower trypsin inhibitor-1 (SFTI-1), one of the smallest naturally occurring [cyclic peptides](#), by 'grafting' an endogenous opioid peptide into its scaffold.

A total of 19 [peptides](#) were chemically synthesized based on the original SFTI-1 blueprint and pharmacologically tested. "One of these variants turned out to be our lead candidate for as potential innovative analgesic molecule, especially for pain in the gastrointestinal tract or in the peripheral organs. This peptide is extremely stable, highly potent and its

action is restricted to the body's periphery. Its use is therefore expected to produce fewer of the typical side-effects associated with opioids," say Gruber and Muratspahić.

The mode-of-action of the peptide is via the so-called kappa opioid receptor; this cellular protein is a drug target for pain relief, but is often associated with mood disorders and depression. The sunflower peptide does not act in the brain, hence there is much less risk of dependency or addiction. Furthermore, it selectively activates only the molecular signaling pathway that influences pain transmission but does not cause the typical [opioid](#) side-effects. The data of the animal model in the current study are very promising: the scientists see great potential for using this peptide in the future to develop a safe medication—which could be administered orally in tablet form—to treat pain in the [gastrointestinal tract](#), and this drug could potentially also be used for related painful conditions, e.g. for inflammatory bowel disease.

The research of this MedUni Vienna laboratory led by Christian Gruber exploits the concept of using nature's blueprint to develop optimized drugs. "We are searching through large databases containing genetic information of plants and animals, decoding new types of peptide molecules and studying their structure, with a view to testing them pharmacologically on enzymes or membrane receptors and ultimately utilizing them in the disease model," explains Gruber. Finally, [potential drug](#) candidates are chemically synthesized in a slightly modified form based on the natural blueprint, to obtain optimized pharmacological properties.

More information: Edin Muratspahić et al, Design of a Stable Cyclic Peptide Analgesic Derived from Sunflower Seeds that Targets the κ -Opioid Receptor for the Treatment of Chronic Abdominal Pain, *Journal of Medicinal Chemistry* (2021). [DOI: 10.1021/acs.jmedchem.1c00158](https://doi.org/10.1021/acs.jmedchem.1c00158)

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