PE-22-28

Molecular Formula: C35H55N11O9

Molecular Weight: 773.9 g/mol | Sequence: GVSWGLR

DESCRIPTION:

PE-22-28 is a spadin derivative that exhibits an improved specificity and affinity for TREK-1 channel compared to spadin. PE-22-28 is a synthetic fast-acting peptide that may treat depression better than other TREK-1 blocking antidepressants such as Citalopram and Paroxetine. PE-22-28 may have the potential to be an impressive compound to treat depression by comparing two studies of mice. The first analysis study concluded, "In vivo, the antidepressant properties of PE 22-28 and its derivatives were demonstrated in behavioral models of depression, such as the forced swimming test. Mice treated with spadin-analogs showed a significant reduction of the immobility time. Moreover, in the novelty suppressed feeding test after a 4-day subchronic treatment PE 22-28 reduced significantly the latency to eat the food pellet" The second application refers to TREK-1 inhibition rather than PE-22-28 itself, results corroborate the conclusion of the first study: "Knockdown of TREK-1 in hippocampal neurons significantly attenuated depressive-like behaviors and prevented the decrease of CUMS [chronic unpredictable mild stress] induced synaptic proteins in mice. Further examination indicated that neuron-specific knockdown of TREK-1 in the hippocampus prevented stress-induced impairment of glutamatergic synaptic transmission in the CA1 region. Moreover, chronic TREK-1 inhibition protects against CUMS-induced depressive-like behaviors and impairment of synaptogenesis in the hippocampus". PE-22-28 may also be effective for treatment of stroke recovery, improved memory and learning.

PROTOCOL:

Content & Potency: 400mcg/0.1ml/spray in nasal spray provided as a 6 ml bottle
Suggested dosage: 1 spray in each nostril once daily

CLINICAL RESEARCH:

Shortened Spadin Analogs Display Better TREK-1 Inhibition, In Vivo Stability and Antidepressant Activity

Depression is a devastating mental disorder that affects 20% of the population worldwide. Despite their proven efficacy, antidepressants present a delayed onset of action and serious adverse effects. Seven years ago, we described spadin (PE 12-28) as a promising endogenous peptide with antidepressant activity. Spadin specifically blocks the TREK-1 channel. Previously, we showed in vivo that spadin activity disappeared beyond 7 h after administration. In order to improve in vivo spadin stability and bioavailability, we screened spadin analogs and derivatives. From the study of spadin blood degradation products, we designed a 7 amino-acid peptide, PE 22-28. In vitro studies on hTREK-1/HEK cells by using patch-clamp technique, showed that PE 22-28 displayed a better specificity and affinity for TREK-1 channel compared to spadin, IC50 of 0.12 nM vs. 40–60 nM for spadin. In the same conditions, we also pointed out that different modifications of its N or C-terminal ends maintained or abolished TREK-1 channel activity without affecting PE 22-28 affinity. In vivo, the antidepressant properties of PE 22-28 and its derivatives were demonstrated in behavioral models of depression, such as the forced swimming test. Mice treated with spadin-analogs

showed a significant reduction of the immobility time. Moreover, in the novelty suppressed feeding test after a 4-day subchronic treatment PE 22-28 reduced significantly the latency to eat the food pellet. PE 22-28 and its analogs were able to induce neurogenesis after only a 4-day treatment with a prominent effect of the G/A-PE 22-28. On mouse cortical neurons, PE 22-28 and its derivatives enhanced synaptogenesis measured by the increase of PSD-95 expression level. Finally, the action duration of PE 22-28 and its analogs was largely improved in comparison with that of spadin, up to 23 h instead of 7 h. Taken together, our results demonstrated that PE 22-28 and its derivatives represent other promising molecules that could be an alternative to spadin in the treatment of depression.

Djillani, A., Pietri, M., Moreno, S., Heurteaux, C., Mazella, J., & Borsotto, M. (2017). Shortened Spadin Analogs Display Better TREK-1 Inhibition, In Vivo Stability and Antidepressant Activity. Frontiers in pharmacology, 8, 643. https://doi.org/10.3389/fphar.2017.00643