Alzheimer’s disease (AD) is the most common form of dementia, which worsens as it progresses, and eventually leads to death. Unfortunately there is no cure for the disease. The medical literature shows that AD is associated with plaques and tangles in the brain. Although AD develops differently in every individual, there are many common symptoms. The cause and progression of AD are still not understood.

The invention relates to peptides and peptidomimetics useful for reducing the neurotoxicity of amyloid peptide aggregates or prion like protein aggregates. The main problem is that an effective means is missing to inhibit Aβ aggregation to toxic oligomers in order to prevent or treat diseases that are the consequence of Aβ aggregation, that is that can be cured by protection against the detrimental effect of Aβ-peptides. Researchers found that members of the novel class of compounds act as β-amyloid structure modifying agents. Therefore, to solve the above outlined problem, the present invention provides a novel group of short peptides and peptidomimetics.

1. *In vitro studies of the neuroprotective effect of the peptides*: The experiments we used 10 ± 1 – week old Wister rats. Anesthesia in experimental animals used chloral hydrate. The brain were quickly removed and immersed in H-ACSF/1 with very low Ca²⁺ and with elevated Mg²⁺ at 4°C. Brain slices (400 μm thick) were prepared from the hippocampus with a McIlwain tissue chopper at 4°C in ice-cold H-ACSF/1 solution.
Results of in vitro studies:

<table>
<thead>
<tr>
<th></th>
<th>Viability 5x excess</th>
<th>Abeta toxicity</th>
<th>2xexcess Viability</th>
<th>Abeta toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>91,3 ± 2,53</td>
<td>53,4 ± 1,49</td>
<td>90,8 ± 0,277/</td>
<td>53 ± 0,529/</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>89,2 ± 1,133/</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>48,8 ± 2,187</td>
<td></td>
</tr>
</tbody>
</table>

The results of the MTT-assay of several novel peptides in two concentrations showed, that the almost peptides studied almost completely eliminated the toxic effect of Aβ.

2. In vivo studies using experimental rat model for electrophysiology:

Extracellular single-unit recordings were performed in rat hippocampus after chloral hydrate anaesthesia. Following a 1 hour recovery period, single-unit activity of the CA1 hippocampal neurons was recorded extracellularly between depths of 2 and 3 mm by means of a low-impedance 7 μm carbon fiber-containing multibarrel microelectrode, and drugs were delivered from surrounding capillary barrels.

Extracellular single-unit recording were obtained from 72 CA1 neurons from a total of 32 anesthetized rats. Pentapeptides were administered i.p. (0.5 mg/100 g) and peristimulus histograms were taken. The data from all 40 min intervals were pooled and mean ± SEM of percentage values were calculated.

These studies indicated that the peptide APAPE protected against the NMDA response-enhancing effect of Aβ 1-42 between ≈ 50 – 250 min after i.p. administration suggesting that APAPE may cross the blood brain barrier.

APAPE peptide proved to show neuroprotective and procognitive effect in a transgenic mouse model of AD (APPsW x PS1 mice, Jackson Labs.) after a 6 month treatment. These early-phase compounds could be therefore considered as drug candidates for neuroprotection in AD.

Keywords

Neurodegenerative disease, Alzheimer’s disease, β – amyloid, peptidomimetics

Benefits

- Application of the new compounds provides nontoxic protein aggregates.
- Reducing the neurotoxicity of amyloid or amyloid-like peptides.
- Provides methods for determining the ability of a compound to inhibit the fibrillation of β-amyloid.
- The compounds can be used in the treatment and/or prevention of neurodegenerative diseases.

Development status

On the basis of the promising preliminary results, researchers currently examine the exact mechanism of the action.

IP status

The Hungarian patent application (P1300317) was submitted in 2013.
PCT examination (PCT/HU2014/000042) was submitted in 2014.

What we are looking for

The University of Szeged is looking for partners to expand the exact mechanism of action and to start ADME/Tox studies to complete the pre-clinical dossier.

Contact

Ms Erika Kamasz
Technology Manager

E-mail: kamasz.erika@rekt.szte.hu
Tel: +(36-62) 546-738