

# Evaluation of symmetric aminoindole-linked triazine for a dual effect on alpha-synuclein and tau isoform 2N4R fibrillization

**Dithiourea derivatives block alpha-synuclein oligomers and fibrils with strong anti-inclusion effects in cells.**

Researchers at Purdue have developed several small molecule inhibitors active at the low micromolar level for alpha-synuclein (alpha-syn) as well as tau isoform 2N4R (T-2N4R) to a limited degree. Both alpha-syn and T-2N4R are heavily associated with the development of Alzheimer's disease in humans. This disease is believed to occur due to accumulation of plaques and intraneuronal neurofibrillary tangles within the brain, causing neural degeneration and eventually death. Currently, no drug exists to treat Alzheimer's disease entirely, only managing some symptoms.

The researchers synthesized a library of compounds with similar chemical motifs and measured their inhibitory activity against development of alpha-syn and T-2N4R oligomers in vitro. Of the 25 compounds synthesized, two significantly inhibited oligomer formation at the low micromolar level.

## **Technology Validation:**

Oligomer inhibition of alpha-syn and T-2N4R measured via photo-inducing cross uncoupled protein (PICUP) assay. It was found that concentrations of 6.25  $\mu$ M - 50  $\mu$ M of the 1st compound and 25  $\mu$ M - 50  $\mu$ M of the 2nd compound significantly reduced alpha-syn oligomer formation. Additionally, a concentration of 50  $\mu$ M of the 1st compound had limited inhibition of T-2N4R oligomers. The 1st compound is capable to disaggregate plaques and tangles isolated from AD patient brains at 50  $\mu$ M.

## **Advantages:**

- Inhibition of oligomer formation and seeding at low micromolar level
- Disaggregation of pre-formed fibrils
- Novel

## **Technology ID**

2023-FORT-70004

## **Category**

Biotechnology & Life  
Sciences/Biomarker Discovery &  
Diagnostics  
Biotechnology & Life  
Sciences/Analytical & Diagnostic  
Instrumentation  
Pharmaceuticals/Other

## **Authors**

Jessica Fortin

## **Further information**

Clayton Houck  
[CJHouck@prf.org](mailto:CJHouck@prf.org)

## **View online**



**Applications:**

- Alzheimer's and Parkinson's disease treatment

- Medical diagnostics

Publication:

Ramirez E, Ganegamage SK, Min S, Patel H, Ogunware A, Plascencia-Villa G, Alnakhala H, Shimanaka K, Tripathi A, Wang KW, Zhu X, Rochet JC, Kuo MH, Counts SE, Perry G, Dettmer U, Lasagna-Reeves CA, Fortin JS. ACS Chem Neurosci. 2023 Nov 1;14(21):3913-3927. doi:

10.1021/acscemneuro.3c00464. Epub 2023 Oct 11. PMID: 37818657 Free PMC article.

<https://pubmed.ncbi.nlm.nih.gov/37818657/>

**TRL:** Pharmaceuticals

**Intellectual Property:**

NATL-Patent, N/A, United States

NATL-Patent, N/A, Europe

Provisional-Gov. Funding, 2023-03-24, United States

PCT-Gov. Funding, 2024-03-21, WO

**Keywords:** Alzheimer's Disease, Inhibitor