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# Application of Diarylhydrazones, Schiff-bases and Their Saturated Derivatives as Multifunctional Inhibitors of Amyloid Self-Assembly

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**Presenter Information**

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**Comments**

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## Application of Diarylhydrazones, Schiff-bases and Their Saturated Derivatives as Multifunctional Inhibitors of Amyloid Self-Assembly

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A new class of multifunctional small molecule inhibitors of amyloid self-assembly is described. Several compounds, based on the diarylhydrazone scaffold were designed. Forty-four substituted derivatives of this core structure were synthesized using a variety of benzaldehydes and phenylhydrazines and were characterized. The inhibitor candidates were evaluated in multiple assays, including the inhibition of A $\beta$  fibrillogenesis and the disassembly of preformed fibrils. The hydrazone scaffold showed strong activity in inhibiting the amyloid beta self-assembly. [1] The structure-activity relationship revealed that the substituents on the aromatic rings had considerable effect on the overall activity of the compounds.

In order to identify possible functional moieties responsible for the strong effect further related compounds (Schiff-bases and their hydrogenated product, secondary amines) were synthesized and tested in the inhibition of fibril formation by Thioflavin-T. Fluorescence spectroscopy and the fibril morphology was followed by Atomic Force Microscopy. The data indicated that the N-N linkage appears important while the importance of the conjugation in the inhibitors could not be confirmed.

[1] B. Török, A. Sood, S. Bag, R. Tulsan, S. Ghosh, D. Borkin, A. R. Kennedy, M. Melanson, R. Madden, W. Zhou, H. LeVine, III, M. Török, *Biochemistry* **2013**, *52*, 1137-1148.