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## Blood-brain Barrier-permeable Fluorone-labeled Dieckols Acting as Neuronal ER Stress Signaling Inhibitors

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### ABSTRACT

We studied the blood-brain barrier (BBB) permeability and intracellular localization of a fluorescein isothiocyanate (FITC)-labeled dieckol (**1**) and a rhodamine B-labeled dieckol (**7**), for exploring the possible therapeutic application of fluorone-labeled dieckols in neurodegenerative diseases. Both compounds (**1** & **7**) were synthesized through a click reaction and were found to be localized in the endoplasmic reticulum (ER) of the two types of brain cell lines (SH-SY5Y and BV-2 cells) tested; they also reduced ER stress in the SH-SY5Y human neuroblastoma cells. In addition, **1** and **7** were shown to pass the BBB in rats upon intravenous administration. Altogether, our study demonstrates, for the first time, that targeted ER-stress reduction in brain cells can be achieved by introducing fluorone-dieckol conjugates into systemic circulation. Therefore, **1** and **7** provide a novel and promising ER-targeting therapeutic strategy for neurodegenerative diseases.

**KEYWORDS:** Fluorone-labeled dieckols | Click reaction | Blood-brain barrier | Endoplasmic reticulum (ER) stress | ER localization

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