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A blend of two resveratrol derivatives abolishes hIAPP amyloid growth and membrane damage

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Abstract.

Type II diabetes mellitus (T2DM) is characterized by the presence of amyloid deposits of the human islet amyloid polypeptide (hIAPP) in pancreatic β-cells. A wealth of data supports the hypothesis that hIAPP's toxicity is related to an abnormal interaction of amyloids with islet cell membranes. Thus, many studies aimed at finding effective therapies for T2DM focus on the design of molecules that are able to inhibit hIAPP's amyloid growth and the related membrane damage as well. Based on this view and inspired by its known anti-amyloid properties, we have functionalized resveratrol with a phosphoryl moiety (4'-*O*-PR) that improves its solubility and pharmacological properties. A second resveratrol derivative has also been obtained by conjugating resveratrol with a dimyristoylphosphatidyl moiety (4'-DMPR). The use of both compounds resulted in abolishing both amyloid growth and amyloid mediated POPC/POPS membrane damage in tube tests. We propose that a mixture of a water-soluble anti-aggregating compound and its lipid-anchored derivative may be employed as a general strategy to prevent and/or to halt amyloid–related membrane damage.

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