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**Phytoalexins as Agents for Insulin Amyloid Fibril Destruction**

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Insulin and its homologs are among the most widely used protein drugs due to their crucial role in treating diabetes. In vivo, insulin can aggregate into amyloid-like fibrils at the injection site. Therefore, studying its amyloid fibrillation mechanism and designing efficient inhibitors are highly important. Phytoalexins are small antimicrobial secondary metabolites produced by plants in response to biological or physical stress. The aim of our study was to investigate the destructive effect of these compounds on the insulin amyloid fibrils using Nile Red fluorescence assay, atomic force microscopy, and circular dichroism spectroscopy. Among tested phytoalexins, only cyclobrassinin and its derivative 2-phenylamino-4,9-dihydro-1,3-thiazino[6,5-b]indole exhibited the highest ability to destroy insulin amyloid fibrils. Our data suggest that these compounds have potential for therapeutic applications in reducing the adverse effects associated with insulin-related long-term treatment of diabetes patients. We gratefully acknowledge the generous support provided by the Slovak Grant Agency VEGA grants 02/0141/25, 01/0347/23 and the Slovak Research and Development Agency under the Contract no. APVV-22-0598.