HPLC–free method of synthesis of isotopically labeled deoxyfructosylated peptides

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The biomarker strategy, based on multiple specific glycation sites in plasma proteins, could essentially increase the efficiency of glycemic control and disease prediction. Besides glycated albumin being a potential biomarker of early states of diabetes mellitus and control of short-term, it has been shown that the glycation of fibrinogen may also impact the formation of the fibrin network, while quantification of glycation of the CD59 protein allows for early detection of glucose intolerance in pregnant women. A different level of glycation of individual lysine residues in proteins has a crucial influence on the stages of the disease. The quantification of new biomarkers of different stages of diabetes requires appropriate isotope-labeled analogs that may improve biomarker search by providing more accurate quantitative data and by more robust detection/quantitation of low-abundance biomarkers. In the presented work, we proposed a fast and simple protocol for the synthesis of isotopically labeled and bi-labeled deoxyfructosylated peptide based on a combination of microwave-assisted synthesis and boronic affinity chromatography using functionalized resin (PhB-Lys(PhB)-ChemMatrix® Rink resin) developed by us. Our method is focused on the synthesis of glycated peptides identified in glycated albumin (GA) after enzymatic hydrolysis catalyzed by trypsin after arginine residues. Thereby, the standard peptides comprised [$^{13}C_6$]-deoxyfructose attached to lysine residue side chain, a dabcyl moiety for determination of standard amounts, and a cleavable linker. Moreover, we applied bi-labeled deoxyfructosylated peptide to determine the concentration of appropriate analog in a sample of human serum albumin glycated in vitro.

Słowa kluczowe

Boronate affinity chromatography, Isotopically labeled, Deoxyfructsylated peptides, Microwave-assisted synthesis, Solid-phase synthesis