

“MGO/MG-H1”は糖化並びに酸化ストレスの早期マーカーである

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Methylglyoxal (MGO) and/or MG-H1 as early biomarkers for glycation and oxidative stress

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Abstract

In the context of Advanced Glycation End-products (AGEs), the term “advanced” refers to the irreversible and structurally stable adducts formed during the final stages of the glycation reaction. These compounds are closely linked to the onset and progression of various chronic diseases influenced by dietary patterns, including diabetes, cardiovascular conditions, and neurodegenerative disorders.

Elucidating the pathways and dynamics of AGE formation is critical not only in clinical chemistry but also in collaboration with food chemistry. Methylglyoxal (MGO), a major precursor of AGEs, is an intermediate metabolite of glycolysis that reacts rapidly and specifically with the guanidino group of arginine residues to form MG-H1 (Methylglyoxal Hydroimidazolone 1). Due to the rapidity and specificity of this reaction, MGO and/or MG-H1 (hereafter referred to as MGO/MG-H1) are attracting attention as early markers of glycation stress.

Moreover, MGO serves as a modulator of oxidative stress by acting as a source of radicals through its interactions with transition metals and impairing mitochondrial function. Additionally, it can promote the generation of reactive oxygen (ROS) via the activation of NADPH oxidase (NOX) through receptor for AGEs (RAGE) signaling.

This review highlights the contributions of three internationally recognized research groups that have significantly advanced the field of MGO/MG-H1 research, with a focus on their impact in both clinical and food chemistry contexts.

Thornalley et al. (UK) laid the groundwork for MGO/MG-H1 research by elucidating non-enzymatic MGO formation pathways, glyoxalase system-mediated detoxification, and the site-specific (hotspot) modifications of MG-H1.

Beisswenger et al. (USA) demonstrated correlations between MG-H1 levels in human blood and urine and decreased glomerular filtration rate (eGFR) and albuminuria, suggesting MG-H1 as an early biomarker of diabetic nephropathy.

Schalkwijk et al. (Netherlands) investigated the role of MGO/MG-H1 in the progression of chronic kidney disease, endothelial dysfunction, and inflammation. Notably, they compiled a comprehensive database of carboxymethyl lysine (CML), carboxyethyl lysine (CEL), and MG-H1 contents in 141 food items and have pioneered dietary intervention studies focused on food-derived AGEs, particularly MG-H1.

This article discusses analytical methods based on the chemical characteristics of MGO/MG-H1, with particular attention to sample preparation in LC-MS/MS analysis and enzyme-linked immunosorbent assay (ELISA) measurements. Based on these technical backgrounds and human-derived data, we emphasize that MGO/MG-H1 should not merely be regarded as precursors to AGEs, but as early markers of glycation and oxidative stress, and more importantly, as “key molecules” linking endogenous metabolism, diet, and disease.