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Determination of Isoaspartate in a Peptide

A fast, inexpensive, and highly accessible method utilizing chemical derivatization and mass spectrometry offers a superior assay for measuring isoaspartate, a key factor in protein degradation and drug instability.

In vitro and in vivo isomerization of aspartate (Asp) to isoaspartate (isoAsp) is one of the main routes to protein degradation. Deamidation of asparagine (Asn) can also yield isoAsp via a common succinimide intermediate. Not only can this transformation change the structure and activity of a protein, it can also lead to immunological response. Furthermore, an increase in endogenous isoAsp has been linked to Alzheimer's disease and aging. The body naturally produces enzymes that work to reduce the levels of isoAsp, namely PIMT and PCMT, both of which methylate isoAsp to encourage isomerization to Asp. The spontaneous, post-translational generation of isoAsp poses an immediate problem to the development of protein-bound pharmaceuticals, where shelf life and activity may be directly affected; in fact, isoAsp generation is one of the most common contributors to heterogeneity in a protein-bound drug. Factors that induce the generation of isoAsp include pH, secondary and tertiary protein structure, and formulation.

Researchers at Purdue University have developed a fast and inexpensive method to determine isoaspartate by chemical derivatization in the backbones of peptides by ionizing labeled peptides. This method is the simplest and most accessible assay for isoAsp determination, which makes it useful to researchers studying its link to disease or drug-bioconjugate degradation.

Advantages:

-Fast

-Inexpensive

-Easily accessible

Potential Applications:

Technology ID

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Category

Biotechnology & Life Sciences/Biomarker Discovery & Diagnostics

Pharmaceuticals/Drug Discovery & Development

Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation

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View online

-Research related to isoAsp's link to disease or drug-bioconjugate degradation

-Medical/Health

-Pharmaceutical industry

TRL: 3

Intellectual Property:

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