Development and Application of Stable Isotope Internal Standard Reagents for Food Safety Testing

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Abstract: This paper introduces the development and application of stable isotope internal standard reagents in the field of food safety testing. Firstly, it discusses the application progress of stable isotope technology in food authenticity identification, food safety traceability, and specific compound analysis. Secondly, it explores the use of multiple isotope internal standards in gas chromatography-mass spectrometry (GC-MS) and ultra-high pressure liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) in environmental monitoring, pharmaceutical analysis, and food safety testing. The synthesis methods of stable isotope-labeled compounds and their applications in drug development, biosynthesis research, and food safety testing are analyzed. Finally, the development methods, application fields, challenges, and the importance of domestic development of deuterium-labeled isotope internal standard reagents are discussed. The paper emphasizes the significant role of stable isotope internal standard reagents in improving the accuracy and sensitivity of food safety testing and anticipates their broad application prospects in this field.

Keywords: Stable isotope internal standard reagents; Food safety testing; Analytical technology

1 Advances

The application of stable isotope technology in food safety testing has seen significant progress in several areas.

In recent years, stable isotope technology has gained widespread application in food authenticity identification and food safety traceability due to its unique advantages. By analyzing the stable isotope composition in food, it is possible to effectively identify the source, processing history, and potential adulteration of food products, thereby ensuring food quality and safety. This technology utilizes the natural abundance differences of stable isotopes in plants and animals from different regions, proving successful in identifying food adulteration and tracing food origins. It not only helps consumers understand the true source of their food but also provides scientific evidence for food safety regulation. [1-3]

Compound-specific isotope analysis (CSIA), a relatively new technique, focuses on the isotopic ratios at the molecular level and has made significant strides in identifying the authenticity of animal and plant-derived foods. This application enhances the accuracy and efficiency of food identification and adulteration detection. Stable isotope dilution analysis (SIDA), known for its efficiency and precision, is widely used as a quantitative method for determining flavor components in food. This technology's development has provided new perspectives and methods for food flavor analysis, aiding in a deeper understanding of food flavor characteristics. [4]

The application of stable isotope mass spectrometry in food adulteration analysis and origin tracing is highly regarded. By accurately measuring the stable isotope composition in food, it is possible to effectively identify instances of food adulteration or misrepresentation of origin, further ensuring food safety. The advancements in stable isotope technology in food safety testing cover multiple aspects, including food authenticity identification, food safety traceability, specific compound analysis, and new areas such as flavor analysis and adulteration detection. These advancements not only enhance the accuracy and efficiency of food safety testing but also provide robust technical support for food safety regulation. [5-7]

2 Application of Multiple Isotope Internal Standard Gas Chromatography-Mass Spectrometry (GC-MS)

Multiple isotope internal standard gas chromatography-mass spectrometry (GC-MS) combines the separation capability of gas chromatography (GC) with the precise identification capability of mass spectrometry (MS) and is widely used in environmental monitoring, food safety, and pharmaceutical analysis. This technology uses isotope-labeled internal standards to correct for matrix effects and losses during the analysis process, thus improving the accuracy and reproducibility of the analysis.

In environmental monitoring, GC-MS is used to detect harmful substances such as sulfides, polycyclic aromatic hydrocarbons (PAHs), and polychlorinated biphenyls (PCBs) in water. These studies demonstrate that GC-MS can provide highly sensitive and selective detection results, aiding in the early warning of odor incidents and the assessment of environmental pollution levels. In food safety, GC-MS is employed to measure chloropropanol content, melamine residues, and β-estradiol residues in food. These studies highlight the crucial role of GC-MS in ensuring food safety and protecting consumer health. [8]

In pharmaceutical analysis, GC-MS is used to detect polybrominated diphenyl ethers (PBDEs) in serum and clenbuterol in pig urine and liver. These applications demonstrate GC-MS's importance in monitoring drug abuse, diagnosing clinical diseases, and conducting pharmacokinetic studies. Additionally, GC-MS is applied in biopharmaceutical research, providing structural information for picogram-level samples, supporting new drug development, and evaluating the safety of existing drugs. The broad application range of multiple isotope internal standard GC-MS offers high-precision and high-sensitivity detection results and effectively addresses complex sample matrix interferences, making it an essential technique in modern analytical chemistry.

3 Application of Ultra-High Pressure Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS)

Ultra-high pressure liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) is an efficient, fast, sensitive, selective, and high-throughput analytical technique widely used in various fields, including but not limited to food safety testing, pharmaceutical research, and environmental monitoring. The following is a detailed analysis of UPLC-MS/MS applications based on the information. [9-10]

Food Safety Testing: UPLC-MS/MS is extensively used in food safety testing, including the detection of pesticide and veterinary drug residues, biological toxins, processing hazards, and food allergens. For example, this technology has been used to simultaneously determine 115 pesticides in blood and detect zearalenone compounds in pork. These studies show that UPLC-MS/MS can provide highly sensitive and accurate results, meeting the needs of food safety testing.

Pharmaceutical Research: In pharmaceutical research, UPLC-MS/MS combines the powerful separation capabilities of ultra-high pressure liquid chromatography with the high sensitivity and specificity of mass spectrometry, becoming an important method for drug analysis. It is widely used in pharmacokinetics, drug component analysis, and drug activity screening. Additionally, this technology is used to analyze drug residues and trace metabolites and to test and analyze traditional Chinese and Western medicines.

Environmental Monitoring: UPLC-MS/MS is also applied in environmental monitoring, such as the simultaneous determination of acidic and basic drugs in wastewater samples. This shows that UPLC-MS/MS has the capability to handle complex samples and extract useful information from them.

Clinical Medicine: In clinical medicine, UPLC-MS/MS supplements traditional diagnostic techniques, providing more accurate and reliable evidence for the precise and rapid diagnosis of many diseases. For instance, the technology is used to detect 25-hydroxyvitamin D3, demonstrating its potential in clinical applications.

Metabolomics and Proteomics: With the development of metabolomics and proteomics, UPLC-MS/MS is increasingly used in biomolecular analysis. Studies have shown that this technology can effectively separate and analyze small and large biomolecules, providing new methods for metabolomics, toxicology, and other research.

Due to its efficiency, speed, sensitivity, and selectivity, UPLC-MS/MS has shown immense potential in various fields. Whether in food safety testing, pharmaceutical research, environmental monitoring, or clinical medicine, UPLC-MS/MS can provide accurate and reliable analytical results, making it an indispensable tool in modern analytical chemistry.

4 Synthesis and Application of Stable Isotope-Labeled Compounds

The synthesis and application of stable isotope-labeled compounds is an interdisciplinary research field involving chemistry, biology, pharmacology, and other disciplines. Stable isotope labeling technology introduces stable isotopes (such as ^{13}C, ^{15}N, ^{2}H) into compounds, enhancing their sensitivity and accuracy in mass spectrometry analysis. This technology is widely used in drug discovery, biosynthesis research, food safety testing, and other areas.

4.1 Synthesis Methods

The synthesis methods of stable isotope-labeled compounds are diverse and include, but are not limited to, the following:

Direct Oxidation: This method utilizes the isotope ^{34}S to synthesize labeled compounds. For instance, ^{34}S-labeled phosphorothioates can be effectively synthesized using this method.

Chemical Synthesis: This involves a series of chemical reactions to introduce stable isotopes (such as ^{13}C, ^{15}N, ^{2}H) into target compounds. For example, ^{13}C-labeled compounds can be obtained via sulfonate ester activation, or deuterium-labeled reagents can be synthesized using deuterated solvents and physical exchange methods.

Biosynthesis: In this approach, stable isotope-labeled precursor substances are used in living organisms to biosynthesize target labeled compounds through biotransformation processes. For example, feeding plants with ^{13}C-labeled precursors allows the study of their metabolic pathways.

4.2 Application Fields

Stable isotope-labeled compounds have extensive applications in various fields:

Drug Development: By labeling drug molecules, researchers can more accurately study their mechanisms of action and metabolic pathways, accelerating the drug development process.

Biosynthesis Research: Stable isotope labeling technology enables in-depth studies of the biosynthetic pathways of secondary metabolites in organisms, providing clues for new drug discovery.

Food Safety Testing: Labeling analysis methods allow for the rapid and accurate detection of harmful residues in food, ensuring food safety.

Environmental Science: Stable isotope labeling is applied in environmental science to trace the migration and transformation of pollutants.

Polymer Material Research: In polymer material research, stable isotope labeling helps study the service performance and environmental degradation properties of materials.

The synthesis and application of stable isotope-labeled compounds is a highly specialized field requiring the selection of appropriate labeling elements and synthesis methods based on different research purposes. With technological advancements and the continuous expansion of new labeling technologies and application areas, stable isotope labeling technology will play an increasingly important role in scientific research and industrial applications.

5 Development and Application of Deuterated Isotope Internal Standard Reagents

The development and application of deuterated isotope internal standard reagents is a complex process involving multiple fields such as chemical synthesis, mass spectrometry analysis, food safety testing, and drug residue detection.

5.1 Importance of Deuterated Isotope Internal Standard Reagents

Deuterated isotope internal standard reagents play an important role in scientific research, particularly in avoiding hydrogen atom interference from ordinary solvents and improving the purity of solvents for nuclear magnetic resonance spectroscopy. They also demonstrate unique value in food safety testing and drug residue detection.

5.2 Synthesis Methods

The synthesis methods of deuterated isotope internal standard reagents mainly include chemical synthesis and physical exchange methods. For instance, different types of deuterium-labeled compounds can be prepared through selective oxidation, alkaline dehydration, and catalytic reactions. The choice of method depends on the nature of the target compound and the required isotope abundance.

5.3 Application Fields

Deuterated isotope internal standard reagents have wide applications in various fields:

Food Safety Testing: For example, in determining the residue levels of β2-agonists in animal urine, the content of xylene musk in edible flavors, and the residues of ciprofloxacin in honey, deuterated isotope internal standard reagents have proven effective and accurate.

Drug Residue Detection: They are used in drug residue detection, forensic toxicology analysis, and other fields.

5.4 Technical Advances and Challenges

Despite the widespread application of deuterated isotope internal standard reagents, their development and application still face challenges. For example, the internal standard reagents used in domestic food safety testing are largely monopolized by foreign companies, limiting the development of related research and technology in China. Developing deuterated internal standard reagents with independent intellectual property rights to reduce reliance on foreign reagents is an urgent issue.

5.5 Importance of Domestic Development

To break the long-term monopoly of foreign companies in the stable isotope labeling reagent field and improve the innovation capability of technologies and products with independent intellectual property rights, domestic research institutions and technology development centers have begun developing urgently needed high-end stable isotope labeling reagent products. These efforts not only help improve the level of chemical pollution monitoring technology in food safety but also promote the strategic transformation and healthy development of the food industry.

The development and application of deuterated isotope internal standard reagents is an interdisciplinary research area involving chemistry, biology, environmental science, and other fields. Continuous technological innovation and domestic development efforts are expected to further broaden its application scope and enhance detection accuracy and efficiency.

6 Conclusion and Outlook

The development and application of stable isotope internal standard reagents hold significant importance in the field of food safety testing. By continuously optimizing detection methods and improving the quality of internal standard reagents, it is possible to effectively enhance the accuracy and sensitivity of food safety testing, providing robust technical support for public health protection. In the future, with further research and technological advancements, the application of stable isotope technology in food safety testing will become more extensive and in-depth.

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