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Advances in Metabolomics based on Mass Spectrometry

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Abstract. Metabonomics, as systems biology's most downstream "omics," is the integrity of the system function change important branch discipline of life. Metabonomics is a research field that focuses on complex biological systems, and there are numerous types of common biological samples, such as biological fluids (urine, saliva, serum, plasma, bile, cerebrospinal fluid, amniotic fluid, tears, pancreatic juice, and intestinal juice, etc.), animal or human tissue (tumor, liver, brain, adipose tissue, etc.), and cells. Metabonomics typically employs two categories of commonly used research methods: mass spectrometry and nuclear magnetic resonance. This paper presents a comprehensive review of the research progress in the field of metabonomics within the medical field. The focus is on disease diagnosis, drug research and development, as well as their relationship to nutrition, toxicology, sports medicine, and other related areas. This review is based on an analysis of mass spectrometry. Despite the significant progress made in science, technology, and research, metabolics research still faces a multitude of challenges and opportunities. The ongoing development and innovation of mass spectrometry technology are crucial for the field's advancement. While mass spectrometry has played a pivotal role in metabolomics research, there is a pressing need to enhance its performance in order to improve sensitivity, resolution, and analysis throughput.

Keywords: Mass Spectrometry, Metabolomics, Disease Diagnosis, Drug Research and Development, Metabolic Changes in Organisms.

1. Introduction

Metabolomics (metabonomics) refers to the overall and dynamic metabolic changes of biological systems caused by biological stimulation, pathophysiological perturbations, or changes in genetic information [1]. Metabonomics is a field of study that enables a more profound comprehension of life processes, the elucidation of disease mechanisms, and the assessment of drug therapy efficacy. As a comprehensive research field, metabolomics not only focuses on the identification and quantitative analysis of metabolites, but also deeply explores their functions and dynamic changes in the organism. The advancement of this area offers a broader range of viewpoints and techniques to investigate the enigmas of existence, and also brings fresh prospects for the prevention and cure of diseases. The employment of metabolites in the examination of intricate biological specimens has displayed considerable advantages, enabling researchers to delve deeper into the metabolic transformations of the body. The application of mass spectrometry allows scientists to precisely identify and quantify metabolites present in biological samples. The accuracy is not only reflected in the metabolite identification, but is embodied in the accurate determination of the content. This allows researchers to capture the subtle variations in the metabolite group, thus a deeper understanding of biological metabolic processes in the body and their association with physiological and pathological states [2].

Metabonomics is a key branch of system biology, focusing on the resolution of all small molecule metabolite dynamics and its inner link with organism physiology and pathology. The research objects of metabolomics are complex biological systems with many types.

The paper reviewed in this study is based on the analysis of mass spectrometry in the field of metabonomics research, and it aims to provide a comprehensive reference for researchers, promote further development and innovation in metabonomics research, and lay the foundation for future applications.

2. Principle of Mass Spectrometry Analysis Technology

Mass spectrometry technology is one of the core technologies in the study of metabonomics, the basic principles involved in the ionization of sample molecules, ion separation, and detection of the mass-to-charge ratio. Sample molecules are ionized into ions in the ion source. This process can be realized through different ionization methods, such as electron bombardment ionization, chemical ionization, laser ionization, etc. For example, rat urine, dog urine, and rat bile can effectively classify sample sources, but the data they produce is not as comprehensive as fluid and temperament and can be used for sample screening. The working process of the mass spectrometry technology consists of several key steps. Firstly, the sample to be analyzed is introduced into the mass spectrometer. Then, through a series of processes such as ionization, the sample molecules are converted into charged particles. These charged particles are then accelerated and separated based on their mass-to-charge ratio. Finally, the separated particles are detected, and the resulting data is analyzed to provide information about the chemical composition and properties of the sample. Each of these steps plays a vital role in ensuring the accuracy and reliability of the mass spectrometry analysis. Recently, the method of combining high-integration and high-throughput microfluidic chips with mass spectrometry has been gradually developed. Lin Jinming et al. have done a lot of work in this regard, combining microfluidic chips with electrospray mass spectrometry technology to study cell analysis and pharmacokinetics, deepening the research on cellular drug metabolism and intercellular signal transmission to the molecular level [3] . The first step is sample pretreatment, which is crucial to ensure the accuracy and reliability of the analytical results. The pretreatment process may involve sample extraction, purification, enrichment and derivatives such as operations, designed to remove interfering substances and enrichment of target metabolites. After undergoing ionization steps, the sample molecules are transformed into ions, thereby ensuring the quality of the subsequent analysis. In this step, ions are accelerated through an electric or magnetic field and then separated, based on their mass-to-charge ratio. Following the signal detection step, ions are detected and recorded through quality analysis. Commonly used signal detectors, including electron multipliers, photo multiplier tubes, and ion counters, etc., are able to the ion signal is converted to electrical signals that can be measured, amplified, and processed. The final step is data analysis, namely the processing and interpretation of mass spectrum data.

Mass spectrometry plays an important role in metabolomics research with its unique principle and workflow. With the continuous enhancement and advancement of mass spectrometry technology, a more profound understanding of the metabolic alterations in organisms and their correlation with physiological and pathological conditions can be gained. This technology serves as a valuable resource in the realms of disease diagnosis and drug research and development, offering a potent solution for scientific investigation.

In metabonomics studies, identification and quantitative analysis constitute the core link of metabolites; their accuracy is directly related to the reliability and validity of research results. Metabolites of appraisal methods mainly include standard comparison, database search and isotope labeling strategies. Standard comparison is a direct and effective method; by comparing the standard with the mass spectra of the sample under test, it can realize the accurate identification of the metabolites. The advantage of this approach lies in its visual and reliability, although it has a limited standard of data acquisition and preparation. Database search is to use the existing database of metabolites, such as

METLIN, and HMDB, then through the mass spectrometry data with the information in the database to identify metabolites. This method possesses the advantages of high flux and automation, but the integrity of the database and the accuracy of appraisal results have important influences on it. The isotope labeling strategy tracks and identifies metabolites by introducing stable isotope tags. This method can improve the identification accuracy and provide dynamic changes of metabolites.

Quantitative analysis of the metabolites is a key link in the study of metabolomics. The commonly used quantitative analysis methods include the internal standard method, the external standard method, the isotope dilution method, etc. Scientific research often employs various quantitative analysis methods to ensure accurate and precise results. One such method is the internal standard method, which involves adding a known concentration of an internal standard substance to the sample during processing and analysis.

Mass spectrometry-based metabolite identification and quantification methods play a pivotal role in metabolomics research. Through continuous optimization and innovation of these methods, a deeper understanding of the metabolic process and mechanism of organisms can be achieved, providing more accurate and comprehensive information for areas such as disease diagnosis and drug research and development.

3. Metabonomics Research Progress

Metabolomics is further divided into Targeted metabolomics and Untargeted metabolomics. Targeted metabolic analysis focuses on quantifying specific metabolites, typically focusing on one or several related metabolic pathways. It is often used to study the pharmacokinetics of drug metabolism to measure the effect of a therapy or genetic modification.

3.1. Association between metabolic pathways and diseases

With the continuous progress of mass spectrometry, metabolics research has made remarkable achievements in revealing the deep relationship between metabolic pathways and various diseases. Roy et al. used UPLC-MS to analyze non-targeted plasma metabolites and targeted metabolites, quantifiable 8 amino acids and 8 acylcarnitine, which are considered biomarkers of cardiovascular disease risk [4] . Vorkas et al. used the UPLC-MS method to conduct non-targeted analysis on the tissues taken from surgical patients with abdominal aortic aneurysms, carotid artery stenosis plaque and femoral artery stenosis plaque, and found that metabolites in the tissues of these patients could be distinguished. It was found that the metabolism related to atherosclerosis included cholesterol metabolism, purine metabolism, pyrimidine metabolism and ceramide metabolism [5] .

In the field of diabetes research, mass spectrometry provides researchers with unprecedented perspectives. Yokoi et al. diagnosed diabetes in rat models by the GC-MS method and found that, compared with normal rats, there were significant differences in asparagine, glutamine, glycerin, kynuretic acid, mannose, taurine, threonine, and tryptophan in rats with spontaneous diabetes mellitus. After 12 weeks of age in spontaneous diabetic rats, the metabolites of the tryptophan metabolism pathway (tryptophan and kynuridine) were significantly reduced, which is a potential biomarker of prediabetes, and the metabolism of tryptophan may be a potential target for diabetic therapeutic intervention. The metabolites of the tryptophan metabolism pathway, specifically tryptophan and kynuridine, underwent a significant reduction. This decrease in these crucial metabolites indicates a potential alteration in the metabolic processes within the bodies of these diabetic rats. The tryptophan metabolism pathway plays a vital role in various physiological functions, and the reduction of its metabolites at this stage in spontaneous diabetic rats could have far-reaching implications for their overall health and the progression of their diabetic condition. It may suggest disruptions in neurotransmitter synthesis, immune function regulation, or other important biological processes that are dependent on an intact tryptophan metabolism pathway. By analyzing biological samples such as the blood and urine of diabetic patients, search. Researchers, by comparing the tumor tissue and normal tissue metabolite spectrum, not only found associated with tumor growth, invasion, and metastasis of specific metabolites but also revealed certain metabolic pathways in cancer drug resistance mechanisms are the key role. These findings for the early diagnosis of cancer, treatment strategy formulation, as well as the new drug research and development provide a strong scientific basis. Metabonomics research not only focuses on the characteristics of single-disease metabolism, but is also committed to revealing a variety of diseases that share common metabolic pathways and markers This cross-disease approach provides new ideas for the development of broad-spectrum therapeutic strategies and preventive measures.

3.2. Application of metabolomics in drug development

Metabolomics has been widely used in the field of drug research and development. Its unique advantage lies in its ability to comprehensively and systematically analyze the effects of drugs on metabolic processes in vivo. Liang et al. evaluated the effect of TCM compounds on myocardial infarction in rats by metabonomics, and found that the therapeutic effect was superior to ginseng and mono-ginseng. Because of the potential efficacy of Chinese herbal compounds in myocardial energy metabolism, changes in urine tricarboxylic acid circulation and pentose phosphate pathways suggest that they may reduce heart damage during myocardial infarction [6] . By comparing the biological in vivo metabolite changes before and after medication, the researchers can deeply understand the mechanism of action of drugs, including how drugs interact with biological metabolic pathways in the body, and how to influence the formation of metabolites and degradation. Metabolomics can not only help identify drug targets, but can also reveal drugs on metabolic pathways of influence on the whole. Wu Yuzheng et al. reviewed the metabolic studies of typical Chinese medicinal materials on diseases [7] . Zhang Aihua et al. reviewed the application of metabolomics in TCM pharmacology, TCM syndromes, TCM prescription syndromes and TCM safety evaluation [8] .

Metabolomics also plays a key role in the elucidation of drug metabolic pathways and the identification of drug metabolites. The metabolic process of drugs in organisms is complex and variable, and a variety of metabolites may be produced. Shi et al. studied the chronic exposure toxicity of acrylamide by means of metabolomics and found three new biomarkers, suggesting that acrylamide can cause lipid and amino acid metabolism disorders and induce oxidative stress [9] . These metabolites may have different pharmacological activities compared to the original drug, and could potentially lead to toxic effects. Metabonomics technology employs a high-flux, sweeping screening approach to analyze metabolites in biological samples, ultimately aiding researchers in gaining a deeper understanding of the metabolic processes of drugs. This technology not only facilitates the prediction of potential toxic effects but also optimizes the design of drugs. As technology progresses and data analysis methods improve, metabonomics is poised to play an increasingly significant role in the field of drug research and development, providing robust support for innovative drug discovery and development.

4. Conclusion

In this review, the latest progress and application of metabolomics based on mass spectrometry are comprehensively summarized from multiple perspectives. Through systematic review and comprehensive analysis, this paper revealed the important role of metabolomics in disease diagnosis, drug development, and other fields. This article undertakes a comprehensive and in-depth exploration to thoroughly summarize the latest and most significant progress as well as the remarkable application results of metabolomics research that is firmly grounded on mass spectrometry across a multitude of diverse fields. Through conducting an exhaustive and meticulous in-depth analysis of its immense value and boundless potential in practical applications, the continuous and further development of metabonomics is earnestly anticipated. It is expected that it will be widely utilized in various domains, thereby providing highly valuable and beneficial references and profound enlightenment. This not only holds great significance for advancing scientific research but also has far-reaching implications for improving healthcare, enhancing agricultural productivity, and promoting industrial innovation. Despite the progress made in science and technology, as well as research, the future of metabolomics research still presents numerous challenges and opportunities. The ongoing development and innovation of mass spectrometry technology is crucial for the field's advancement. While mass spectrometry has played a significant role in metabolomics research, there is a need to improve and optimize its performance to enhance the sensitivity, resolution, and throughput of the analysis. By constantly promoting the development of these areas, it is expected that further research in metabonomics will inject new vitality and broad application.

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