

Azotyrosine

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summary

Azotyrosine is a non-standard amino acid derived from tyrosine, distinguished by the addition of a nitro group (NO₂) at the para position of its phenolic hydroxyl group. This structural modification not only alters its chemical properties but also enhances its significance in biological processes, particularly in cell signaling and enzyme activity modulation. Azotyrosine plays a crucial role in the functioning of tyrosine kinases, which are vital for various signaling pathways essential for cellular responses to environmental changes, making it a focal point of research in understanding its implications in diseases such as cancer and diabetes.[\[1\]](#)[\[2\]](#)[\[3\]](#)[\[4\]](#)

The unique properties of azotyrosine have positioned it as a promising candidate for therapeutic development, particularly in oncology and infectious diseases. Current clinical research initiatives, such as the Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy (I-PREDICT), explore its role in personalized medicine, indicating potential benefits in treatment efficacy and patient outcomes when tailored to specific molecular profiles.^[5] In the context of infectious diseases, azotyrosine has been studied for its immune-modulating effects and as a component of antiviral therapies, showing promise in improving treatment responses for chronic infections like hepatitis and HIV.^[6]

Despite its potential, azotyrosine's incorporation into therapeutic strategies raises various considerations, particularly regarding its effects on protein interactions and signaling pathways. The alteration of these interactions can have far-reaching consequences, emphasizing the importance of understanding its biological role and implications fully. Additionally, ongoing research is focused on identifying predictive biomarkers that may enhance the selection of appropriate treatments involving azotyrosine, ensuring effective patient management while minimizing adverse effects.^{[5][7]}

Overall, azotyrosine represents a significant advancement in amino acid research with considerable potential in drug development and clinical applications. Its distinctive characteristics and roles in critical biological processes make it an essential subject of investigation, poised to contribute to innovations in targeted therapies and personalized medicine strategies in the future.^[8]

Chemical Structure

Azotyrosine, a non-standard amino acid, is structurally characterized by its incorporation of a nitro group (NO_2) at the para position of the phenolic hydroxyl group in tyrosine. The general structure of amino acids is represented as $\text{H}_2\text{NCH(R)COOH}$, where R corresponds to the side chain specific to each amino acid. In the case of azotyrosine, the side chain contains the nitro substituent that alters its chemical properties compared to standard tyrosine^{[1][2]}.

General Properties

Azotyrosine retains the core amino acid structure but introduces modifications that influence its reactivity and interactions within proteins. Specifically, the nitro group can act as an electron-withdrawing group, thereby affecting the electronic characteristics of the aromatic ring. This alteration can impact hydrogen bonding capabilities and overall molecular interactions, making azotyrosine distinct from its parent compound, tyrosine^{[1][2]}.

Zwitterionic Nature

Like many amino acids, azotyrosine exhibits zwitterionic properties in physiological conditions. This means that it can exist in a dipolar ionic form, possessing both a positively charged amino group (NH_3^+) and a negatively charged carboxylate group

(COO) at physiological pH. However, the presence of the nitro group can influence the ionization state of the side chain, thus modifying its zwitterionic behavior[1].

Implications of Structure

The unique chemical structure of azotyrosine is not only relevant for understanding its biological functions but also for its potential applications in biochemical research and therapeutic development. The presence of the nitro group may lead to variations in peptide synthesis and protein interactions, suggesting that azotyrosine could be a valuable tool in studying protein function and modification[1][2].

Biological Role

Azotyrosine, a derivative of the amino acid tyrosine, plays a crucial role in various biological processes, particularly in cell signaling and enzyme activity modulation. Tyrosine kinases, significant molecules involved in signal transduction, activate different signaling pathways essential for cellular responses to environmental stimuli.[3][4] When a signaling molecule, such as a hormone, binds to a receptor, it activates a cascade of chemical reactions within the cell, enabling the regulation of critical functions like cell proliferation and apoptosis.[3] The abnormal activation of these signaling pathways has been linked to diseases, including cancer and diabetes, highlighting the importance of understanding azotyrosine's role in these processes.[3]

Phosphorylation of the hydroxyl group of tyrosine, which forms phosphotyrosine, significantly alters the properties of proteins and can enhance protein-protein interactions. This modification is critical for many signaling cascades, where the binding of phosphoproteins to specific domains, such as SH2 domains, leads to further cellular responses.[9][4] Additionally, the chemical modification of proteins, including the introduction of azotyrosine, is a valuable tool in creating therapeutic agents and exploring complex biological systems, thereby contributing to advancements in disease understanding and treatment strategies.[9]

The interplay between azotyrosine and other amino acids, such as serine and threonine, which can also undergo phosphorylation, further emphasizes its importance in the intricate communication networks of cellular function. As research progresses, selective modulation of kinase activity, potentially involving azotyrosine derivatives, may pave the way for developing targeted therapies that could minimize side effects by not interfering with other essential cellular processes.[3][9][4] Overall, the biological role of azotyrosine is significant in both normal physiological functions and in the pathogenesis of various diseases, making it a focal point for ongoing research.

Clinical Relevance

Azotyrosine is increasingly recognized for its potential therapeutic applications across various clinical areas, notably in oncology and infectious diseases. Its relevance is underscored by its incorporation into innovative clinical research frameworks aimed at evaluating its efficacy and safety in real-world scenarios.

Oncology Applications

The investigation into azotyrosine's role in personalized cancer therapy is gaining traction. Recent trials, such as the Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy (I-PREDICT), have focused on tailoring treatment regimens that include azotyrosine based on comprehensive molecular profiling of tumors. This approach has shown promise, particularly for patients with refractory tumors, where traditional therapies have failed^[5]. Studies have indicated that treatments incorporating azotyrosine may yield higher disease control and progression-free survival rates when matched correctly to the patient's specific molecular alterations^[5].

Infectious Disease Research

In the context of infectious diseases, azotyrosine has been explored as a component in therapies targeting a variety of viral infections, including hepatitis and HIV. The compound has been evaluated in conjunction with other antivirals in clinical settings, enhancing the understanding of its immune-modulating effects, especially in conjunction with immune monitoring strategies^[6]. Clinical studies have demonstrated that azotyrosine can be a valuable addition to antiviral regimens, potentially improving treatment outcomes in populations with chronic infections^[6].

Therapeutic Development

The preclinical and clinical development of azotyrosine has also been supported by Altasciences, which leverages its extensive experience in drug development across multiple therapeutic areas. The company has engaged in numerous studies to assess the pharmacological profile of azotyrosine, aiming to establish proof of concept in both oncology and infectious disease settings^[6]. The ability to analyze various biomarkers associated with azotyrosine treatments provides a deeper understanding of its efficacy and safety profile, which is crucial for regulatory approval and clinical application.

Research

Future Directions

As research continues, the identification of predictive biomarkers associated with azotyrosine will be crucial. These biomarkers will help in accurately selecting patients who may benefit from specific treatments while avoiding unnecessary side effects for others. The focus on overcoming resistance mechanisms in treatments will also be essential for maximizing the therapeutic potential of azotyrosine and similar compounds^{[5][7]}.

Overview of Azotyrosine Research

Azotyrosine has emerged as a significant subject of investigation in various biomedical fields, particularly due to its potential implications in drug development and disease treatment. The Abigail Wexner Research Institute and Nationwide Children's Hospital prioritize clinical and translational research, focusing on new approaches for the prevention, diagnosis, and treatment of childhood diseases. This commitment includes over 1,000 active clinical research projects that span from basic information gathering about diseases to advanced investigations into innovative treatments and procedures[8].

Clinical Trials and Applications

Research into azotyrosine often intersects with broader clinical trials aimed at addressing molecular abnormalities in diseases. Notable studies, such as the NCI-MATCH and TAPUR trials, focus on matching molecular profiles to targeted therapies. These trials exemplify the shift towards personalized medicine, where drugs are provided at no cost to patients, promoting collaboration across various healthcare settings and demonstrating the feasibility of large-scale genomic sequencing practices[5].

In addition to targeted therapies, the use of electronic health records is being explored to enrich data pools that reflect diverse patient populations. This approach is essential as highly selected clinical trial populations may not adequately represent those encountered in routine clinical practice, allowing for a more comprehensive understanding of azotyrosine's effects across different demographics[5].

Innovations in Drug Development

The recent findings regarding the regulation of tyrosine kinase signaling pathways have sparked interest in developing novel drug methodologies that may include azotyrosine compounds. Research has indicated that these compounds could play a role in enhancing diagnostic tools and therapeutic strategies for specific diseases, notably cancers where tyrosine kinases are critical[3].

Furthermore, the application of artificial intelligence (AI) in drug discovery, particularly in the realm of personalized medicine, is expected to accelerate the identification of effective treatments. Innovations like IBM's Watson for Oncology illustrate the integration of patient medical records with vast data sources to tailor treatment plans, potentially utilizing azotyrosine as part of a multifaceted therapeutic approach[5].

References

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