O-Methyltyrosine

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summary

O-Methyltyrosine, also known as metyrosine, is a chemical compound with the molecular formula C10H13NO3, notable for its role as a competitive inhibitor of the enzyme tyrosine hydroxylase. This inhibition significantly reduces the synthesis of catecholamines, including dopamine, norepinephrine, and epinephrine, which are critical neurotransmitters involved in numerous physiological processes. The compound has gained prominence in both biochemical research and medical applications, particularly for its use in treating conditions related to catecholamine overproduction, such as pheochromocytoma, a tumor of the adrenal gland that leads to excess catecholamine secretion and related symptoms like hypertension and tachycardia.[1][2][3]

O-Methyltyrosine exhibits a range of physical and chemical properties that enhance its utility in medical and research settings. It is typically found as a crystalline solid with a melting point of 124-126 °C and a boiling point of approximately 348.2 °C.[1][2] The compound is synthesized mainly through methylation of tyrosine, utilizing various catalytic methods that have evolved to improve yield and sustainability.[4][5] Its structural modification compared to tyrosine alters its solubility and reactivity, factors that are critical for its bioavailability and interaction with biological systems.[1][3]

The medical applications of O-Methyltyrosine extend beyond pheochromocytoma, as its mechanism of action has implications in managing conditions associated with dysregulated neurotransmitter systems, including hypertension and anxiety disorders.[6][7] Despite its therapeutic benefits, the compound is associated with potential side effects such as sedation, dizziness, and gastrointestinal disturbances, necessitating careful monitoring and dosage adjustments under medical supervision.[6][8] The increasing interest in O-Methyltyrosine highlights its significance in pharmacology and potential future applications in metabolic engineering and psychiatric conditions.[9][10][11]

O-Methyltyrosine's regulatory status is defined by various compliance requirements related to its manufacture and distribution, including the necessity for Certificates of Analysis (COA) to confirm its purity and identity. This regulatory oversight ensures that O-Methyltyrosine is utilized safely and effectively in both clinical and research contexts, underscoring its relevance in contemporary biomedical science.[12][13][14]

Properties

O-Methyltyrosine, also known by its chemical formula C10H13NO3 and CAS number 6230-93-9, possesses various chemical and physical properties that contribute to its application in biochemical research and medicine.

Physical Properties

O-Methyltyrosine is typically encountered as a crystalline solid with specific melting and boiling points that are relevant for its handling and application. The melting point is documented to be around 124-126 °C, while the boiling point is reported to be approximately 348.2 °C[1][2]. These thermal properties are significant for determining the conditions under which the compound can be effectively utilized.

Chemical Structure

The molecular structure of O-Methyltyrosine features a phenolic ring, characteristic of tyrosine derivatives, with a methyl group substituting the hydroxyl group on the aromatic ring. This structural modification alters its solubility and reactivity compared to its parent compound, tyrosine[1][3].

Purity and Quality

The purity of O-Methyltyrosine is critical in both research and pharmaceutical applications. Product specifications include acceptable quality ranges that are established to ensure consistency and efficacy in usage. Certificates of Analysis (COA) are available to confirm the purity and identity of the compound, providing vital information for regulatory compliance[14].

Solubility and Stability

O-Methyltyrosine's solubility in various solvents affects its bioavailability and practical applications. It is known to be soluble in polar solvents, and its stability is influenced by factors such as pH and temperature. The compound's properties are also assessed in relation to its interaction with biological systems, particularly in studies involving neurotransmitter synthesis and metabolism[15][4].

Synthesis

O-Methyltyrosine (H-Tyr(Me)-OH) can be synthesized through various chemical pathways, often involving the modification of the amino acid tyrosine. One prominent method involves the use of O-methylation processes, where the hydroxyl group of tyrosine is methylated to produce O-methyltyrosine. This reaction can be catalyzed by methylating agents, which facilitate the transfer of a methyl group to the hydroxyl group of the tyrosine molecule[4][5].

Additionally, advances in synthetic methodology have improved the efficiency and yield of O-methyltyrosine production. For instance, the use of specific reaction conditions, including temperature and pH control, has been shown to enhance the selectivity of the methylation reaction[16]. Furthermore, the development of new catalysts and solvents has enabled more sustainable synthesis pathways, reducing the environmental impact of the production process[17].

In the context of biochemistry, O-methyltyrosine has also been explored for its potential roles in metabolic engineering and as a precursor in the synthesis of other bioactive compounds. Its incorporation into metabolic pathways can be influenced by enzymatic reactions that utilize similar substrates, highlighting its importance in both synthetic and biological frameworks[1].

Biological Role

O-Methyltyrosine (OMT) plays a significant role in the biosynthesis and regulation of neurotransmitters within the nervous system. As a competitive inhibitor of the enzyme tyrosine hydroxylase, OMT reduces the conversion of tyrosine into L-DOPA, the precursor for dopamine, norepinephrine, and epinephrine. This inhibition subsequently leads to decreased synthesis of these catecholamines, which are crucial for various physiological processes including mood regulation, stress response, and overall neurotransmitter balance in the body[18][19][20].

In addition to its role in catecholamine synthesis, OMT also appears to affect serotonergic activity in the brain. Studies have suggested that the depletion of catecholamines caused by OMT administration may lead to an increase in serotonergic activity, although the precise mechanisms of this interaction remain to be fully elucidated[21][22]. The modulation of neurotransmitter levels by OMT underscores its potential implications in the treatment of conditions associated with dysregulated neurotransmitter systems, such as hypertension and anxiety disorders[6].

Furthermore, OMT's involvement in the physiological actions of norepinephrine and dopamine highlights its significance in motivated behaviors. Norepinephrine, which is synthesized from dopamine, is critical in regulating attention and arousal, influencing how organisms respond to motivational stimuli[23][24]. By affecting the biosynthesis of these key neurotransmitters, OMT can have far-reaching effects on behavioral and physiological responses, making it a molecule of interest in both pharmacological and physiological studies[9][10][11].

Medical Applications

O-Methyltyrosine, also known as metyrosine, is primarily used in the medical field as an adjunct treatment for certain conditions related to catecholamine overproduction. It acts as an inhibitor of tyrosine hydroxylase, thereby decreasing the synthesis of catecholamines such as dopamine, norepinephrine, and epinephrine. This mechanism is particularly beneficial for managing pheochromocytoma, a tumor of the adrenal gland that leads to excess catecholamine secretion, causing symptoms such as hypertension and tachycardia[7][6].

Indications and Efficacy

Metyrosine is indicated for use in patients with inoperable pheochromocytoma or in cases where surgery is not feasible. By reducing catecholamine levels, metyrosine can help control symptoms associated with this tumor, thus improving the quality of life for affected individuals. In clinical settings, its efficacy has been demonstrated in managing severe hypertension and associated symptoms in patients with pheochromocytoma, especially in preparation for surgical intervention[25].

Dosage and Administration

The dosage of metyrosine can vary based on individual patient needs and the severity of catecholamine overproduction. It is essential that treatment with metyrosine be conducted under strict medical supervision, as adjustments may be necessary

based on therapeutic response and potential side effects. Patients are advised to maintain close communication with healthcare providers, who will consider factors such as drug interactions and pre-existing health conditions before prescribing this medication[6].

Potential Side Effects

While metyrosine can be effective, it may also cause side effects including sedation, dizziness, and gastrointestinal disturbances. Patients should be monitored for these adverse effects, and any concerns should be discussed with a healthcare professional. As with any medication affecting neurotransmitter synthesis, there is also the potential for interactions with other drugs, highlighting the importance of a thorough medication review before initiation[7][17].

Pharmacology

O-Methyltyrosine, also known as metyrosine, is a medication primarily used in the treatment of certain types of tumors, specifically pheochromocytoma and paraganglioma, which produce excess catecholamines. Its pharmacological effects are closely related to its mechanism of action, which involves the inhibition of tyrosine hydroxylase, the enzyme responsible for the conversion of tyrosine to L-DOPA, a precursor to dopamine and subsequently norepinephrine and epinephrine [8][26].

Dosage and Administration

The dosage of O-Methyltyrosine can vary based on individual patient needs and response to therapy. It is crucial to monitor urinary catecholamine levels to adjust the dosage appropriately [8]. During treatment, patients are hospitalized for close monitoring, especially during initial dose adjustments [8].

Mechanism of Action

By inhibiting tyrosine hydroxylase, O-Methyltyrosine decreases the synthesis of catecholamines, leading to reduced levels of norepinephrine and epinephrine in the body. This is particularly beneficial in managing symptoms associated with catecholamine excess, such as hypertension, tachycardia, and anxiety [6][8]. As a result, patients often experience a significant improvement in clinical symptoms, including a decrease in urinary metanephrine and normetanephrine levels [8].

Pharmacokinetics

O-Methyltyrosine is relatively metabolically stable, which allows it to maintain effective plasma levels for therapeutic action. It is absorbed well when administered orally and exhibits a good bioavailability profile [27][26]. The drug is typically administered in conjunction with ±blockers to further enhance blood pressure control [8].

Side Effects

As with any medication, O-Methyltyrosine is associated with potential side effects, including drowsiness, dizziness, dry mouth, and gastrointestinal disturbances such as diarrhea [6][8]. Serious adverse reactions, while rare, can occur and include severe allergic reactions and significant alterations in mental status or kidney function. Patients are advised to report any concerning symptoms to their healthcare provider immediately [6].

Regulatory Status

O-Methyltyrosine, a compound utilized primarily in medical contexts, is subject to various regulatory considerations concerning its use, manufacturing, and distribution.

Certificates of Origin (COO)

The Certificates of Origin (COO) are crucial for confirming the country of manufacture of O-Methyltyrosine. These certificates detail the materials and components used in the production process, indicating whether they are derived from natural, synthetic, or other specific sources. Such documentation is essential for ensuring compliance with customs, trade, and regulatory standards, which may vary by region and application.[12][13].

Safety Data Sheets (SDS)

For O-Methyltyrosine, Safety Data Sheets (SDS) provide comprehensive safety information regarding the handling, storage, and disposal of the product. The SDS is a key document for regulatory compliance, ensuring that users are aware of potential hazards and safe practices associated with the compound.[12].

Product Specifications (PS)

Product Specifications (PS) for O-Methyltyrosine offer an in-depth breakdown of the compound's properties, including its chemical composition, physical state, purity, and storage requirements. The PS also outlines acceptable quality ranges and the intended applications of O-Methyltyrosine, which is critical for regulatory approvals and market distribution.[12][14].

Certificates of Analysis (COA)

Certificates of Analysis (COA) serve as quality assurance documents that confirm the identity, strength, and purity of O-Methyltyrosine. These certificates can be accessed by entering the product’s Lot Number, which is important for compliance with regulatory requirements in various markets. The Lot and Batch Numbers are typically indicated on the product label, enabling traceability and quality control in the supply chain.[12][13][14].

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