Nicotinylamino acid

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summary

Nicotinylamino acids, a group of chemical compounds characterized by the presence of an amino acid structure linked to a nicotinic acid moiety, play significant roles in various biological and industrial applications. Notably, niacin (vitamin B3), a prominent member of this group, is crucial for numerous metabolic processes, including energy metabolism and neurotransmitter synthesis, underscoring its importance in human health.[1][2] Due to their diverse functional properties, nicotinylamino acids have garnered attention in fields ranging from pharmaceuticals to cosmetics, where they are utilized for their moisturizing, skin-conditioning, and therapeutic effects.[3][4][5]

The structural diversity of nicotinylamino acids allows for tailored applications, with variations in the R group influencing solubility, reactivity, and biological function.-[6] This adaptability enables their incorporation in various formulations, including creams, gels, and dietary supplements, aimed at enhancing skin health and treating nutritional deficiencies.[4][6][7] Their biosynthesis, primarily starting from the amino acid ornithine, reflects a complex interplay of biochemical pathways that leads to the production of nicotine and its derivatives, emphasizing their relevance in natural product synthesis.[8]

However, the use of nicotinylamino acids is not without controversy. Clinical research has indicated potential adverse effects, such as flushing associated with high doses of niacin, which raises concerns regarding its safety in specific populations, particularly individuals with preexisting health conditions.[9][10] Furthermore, there are implications of decreased glucose tolerance in patients using niacin, necessitating careful monitoring of blood sugar levels.[11][9] These concerns highlight the need for ongoing research to ensure the safe and effective use of nicotinylamino acids in both therapeutic and cosmetic applications.

Chemical Structure

The chemical structure of Nicotinylamino acids is characterized by a backbone that includes an amino acid structure, where the central carbon atom is bonded to a

hydrogen atom, an amino group, a carboxylic acid group, and a distinctive R group or side chain that varies among different amino acids[1].

Functional Groups

In terms of functional groups, the Nicotinylamino acids can contain different chemical entities such as hydroxyl groups, alkoxy groups, and carboxyl groups, which play significant roles in their reactivity and biological activity. For example, they may feature methoxy groups or hydroxy acids, contributing to their chemical behavior in various applications, including topical formulations[3][4].

General Formula and Substituents

Compounds of the general formula I and their salts can be synthesized using established methods in peptide chemistry. This process may involve the complete synthesis of the compound, the removal of protective groups, alkylation of free amino groups, or modifications of carboxyl groups[3]. Additionally, the compounds can be modified by incorporating various substituents on the alkyl or aryl residues. These substituents can include halogen, amino, hydroxy, C1-C6 alkoxy, and several others, which enhance the functional properties of the molecules[3][5].

Molecular Diversity

The diversity in the R group structure contributes to the unique properties of each Nicotinylamino acid, affecting their solubility, reactivity, and biological functions. This variability allows for the tailoring of these compounds for specific applications, including cosmetic and pharmaceutical products, where their incorporation may range from concentrations of 0.5 to 5,000 ppm in topical preparations[5][6].

Properties

Composition and Formulation

Nicotinylamino acids can be formulated in various galenic forms, such as creams, lotions, gels, emulsions, and powders[4]. The compositions may also include additional functional ingredients that enhance their efficacy, with the distinction between "active" and "functional" ingredients being context-dependent[4]. Typical formulations may contain between 25% to 90% water, with a preference for 40% to 80% by weight, depending on the intended application[4].

Emulsifiers and Particulate Materials

The preferred formulations of nicotinylamino acids utilize water-in-silicone emulsions, which require emulsifiers to stabilize the mixture. The emulsifiers are typically present in amounts ranging from 0.1% to 10% by weight[4]. Additionally, particulate materials

such as pigments and powders can be incorporated, with concentrations of 0.01% to 20% by weight, to achieve specific aesthetic or functional properties[4][5].

Active and Additional Ingredients

The compositions may also encompass various conventional and non-conventional ingredients that provide benefits such as skin conditioning, moisturizing, or sun protection[4]. Nonlimiting examples include thickeners, surfactants, and antioxidants. The choice of ingredients, both active and additional, is tailored to the desired product characteristics and application area[4].

Synergistic Effects

Nicotinylamino acids demonstrate potential synergistic effects when combined with other ingredients, enhancing their therapeutic outcomes. For instance, the simultaneous use of homarine and erythritol in formulations has been noted for their benefits in treating skin dehydration[4]. Such combinations exemplify how the formulation of nicotinylamino acids can be optimized for improved skin health outcomes.

Biosynthesis

The biosynthesis of nicotinylamino acids involves several intricate biochemical pathways, primarily starting from the amino acid ornithine. The initial step is the decarboxylation of ornithine by ornithine decarboxylase (ODC), which produces putrescine.[8] Putrescine is subsequently methylated to form N-methyl putrescine through the action of putrescine N-methyltransferase (PMT), utilizing S-adenosyl-methionine (SAM) as a methyl donor. Following this, N-methyl putrescine undergoes deamination to yield 4-methylaminobutanal, catalyzed by the enzyme N-methyl putrescine oxidase (MPO). This intermediate then spontaneously cyclizes to produce the N-methyl-”1pyrrollidium cation, a key precursor in the synthesis of nicotine and its derivatives.[8]

The final step in the biosynthetic pathway of nicotine is the coupling of the N-methyl--”1pyrrollidium cation with nicotinic acid. While research has confirmed that some form of coupling occurs between these two structures, the precise mechanism remains elusive. Current hypotheses suggest that nicotinic acid is converted into 2,5-dihydropyridine through 3,6-dihydronicotinic acid, with this intermediate subsequently reacting with the N-methyl-”1pyrrollidium cation to yield enantiomerically pure ( )-nicotine[8]

This biosynthetic process highlights the complex interrelations of amino acid metabolism and alkaloid formation, reflecting broader themes in the study of natural product synthesis and metabolic pathways.

Biological Role

Nicotinylamino acids, particularly in the form of niacin (vitamin B3), play a crucial role in various biological functions within the human body. They are vital for the synthesis

of nicotinamide adenine dinucleotide (NAD) and its phosphorylated form, NADP, both of which are essential cofactors in numerous metabolic processes.[2]

Energy Metabolism

NAD functions primarily in catabolic reactions, where it helps transfer the potential energy derived from carbohydrates, fats, and proteins into adenosine triphosphate (ATP), the cell's primary energy currency.[2][12] This conversion is essential for cellular energy production, enabling cells to perform necessary functions. NADP, on the other hand, is involved in anabolic reactions, including the synthesis of fatty acids and cholesterol, as well as maintaining cellular antioxidant capacity.[2]

Immune Function and Structural Support

Nicotinylamino acids also contribute to the immune response by supporting the production of antibodies and protecting the intestinal barrier against pathogens.[2][1] Additionally, amino acids, which are the building blocks of proteins, provide structural support throughout the body, exemplified by collagen, the most abundant protein in connective tissues.[2]

Neurotransmitter Synthesis

Nicotinylamino acids are integral to the synthesis of neurotransmitters, chemical messengers that transmit signals within the nervous system.[13][1] Certain amino acids influence the levels of specific neurotransmitters, potentially aiding in the management of conditions like attention-deficit hyperactivity disorder (ADHD).[13][1] For instance, compounds such as acetyl-L-carnitine and glycine may support neurotransmitter function, thereby impacting mood and cognitive processes.[13]

Disorders and Health Implications

Disruptions in nicotinylamino acid metabolism can lead to various health issues, including metabolic and cardiovascular diseases.[14][15] Additionally, deficiencies can result in conditions such as pellagra, which affects the nervous system and can lead to symptoms like lethargy and confusion due to energy deprivation at the cellular level.[16][17] Hence, maintaining adequate levels of nicotinylamino acids is crucial for overall health and proper bodily function.

Applications

Nutraceutical and Pharmaceutical Uses

Nicotinylamino acid is utilized in various formulations aimed at enhancing skin health and treating conditions such as cutaneous dehydration. The combination of homarine and erythritol has been shown to exhibit osmo-protective effects, making it beneficial in formulations designed to combat the signs of skin dehydration caused by environ-

mental, psychological, and hormonal factors[4]. Such formulations can help maintain skin suppleness and barrier function, thereby supporting the underlying dermis and mitigating the effects of skin aging[4].

Cosmetic Industry

The cosmetic market is increasingly integrating nicotinylamino acid due to its moisturizing properties. It is often combined with occlusive substances to delay water evaporation, humectants to capture atmospheric moisture, and other skin-conditioning agents[4]. In addition to moisturizing benefits, it may also act as a keratolytic agent, promoting exfoliation and improving overall skin texture[4]. Various moisturizing products in the market leverage these attributes to offer alternatives for maintaining flexible and soft skin regardless of age[4].

Clinical Research

Effects on Glucose Tolerance

Clinical trials have demonstrated that niacin can lead to decreased glucose tolerance in patients, prompting recommendations for careful monitoring of individuals with diabetes or those at risk of developing the condition. The American College of Cardiology/American Heart Association (ACC/AHA) cholesterol management guidelines advocate for pre-treatment fasting blood glucose and glycosylated hemoglobin (HbA1c) assessments, along with regular monitoring every six months during therapy. If hyperglycemia is noted, adjustments to niacin dosage or concurrent antidiabetic medications may be necessary, with discontinuation of niacin advised if high blood sugar levels persist[11][9].

Clinical Trials Registry

Nicotinylamino acids, including niacin, are documented in the ClinicalTrials.gov registry, which provides comprehensive information about ongoing and completed studies on this compound. Each entry outlines the study's objectives, participant criteria, and locations, facilitating transparency and access to research findings in human health[9].

Cardiovascular Studies

The Familial Atherosclerosis Treatment Study (FATS) investigated the efficacy of niacin in patients with established coronary artery disease. In this study, participants who received niacin in conjunction with colestipol exhibited a lower rate of disease progression in coronary arteries compared to those receiving conventional therapy alone. Specifically, only 25% of patients in the niacin group experienced disease progression, while 39% showed regression, highlighting the potential benefits of niacin in cardiovascular health[16].

Adverse Reactions

The administration of niacin is commonly associated with flushing episodes, characterized by sensations of warmth, redness, and tingling. In pivotal studies of NIASPAN, these flushing reactions were reported by up to 88% of participants, with some experiencing additional symptoms like dizziness and palpitations. Notably, these reactions led to a discontinuation rate of approximately 6% among patients[18].

Dietary Supplementation

Nicotinylamino acid is also acknowledged for its role as a dietary supplement. It is recognized for its contribution to maintaining adequate nutrient levels, particularly in scenarios where dietary intake may be insufficient, such as during specific life stages-[7]. Supplementation can help address deficiencies and enhance overall health when combined with a balanced diet[7].

Special Dietary Protocols

In more specialized dietary contexts, such as the Elemental Diet aimed at severe malnutrition recovery, nicotinylamino acid can play a critical role. This diet relies on providing essential nutrients in forms that are easily absorbed, which may include amino acids and vitamins[2]. Such protocols emphasize the importance of comprehensive nutrient support, particularly for individuals with significant dietary restrictions or absorption issues[2].

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Safety and Precautions

Nicotinamide, a form of niacin (B3), is associated with a lower incidence of side effects compared to its counterpart, nicotinic acid. Nonetheless, when consumed in high doses, it may cause adverse effects including nausea, vomiting, stomach discomfort, headache, fatigue, dizziness, and rash.[10] Severe cases can lead to liver toxicity, underscoring the importance of adhering to recommended dosages and consulting a healthcare provider if any troubling symptoms arise.[10]

Drug Interactions

Nicotinamide may interact with several medications, necessitating caution during concurrent use. For instance, it may increase the plasma levels of carbamazepine, an anti-seizure medication, by reducing its metabolic clearance.[10] Additionally, it has the potential to enhance the anticoagulant effects of blood thinners, such as warfarin, which could pose a risk of excessive bleeding.[10] Other medications like primidone, used for epilepsy, may also have altered efficacy due to nicotinamide's impact on drug metabolism.[10]

Special Populations

It is vital for individuals with certain medical conditions to consult their healthcare provider before initiating nicotinamide supplementation. Those with liver disease, bleeding disorders, or a history of adverse reactions to niacin should be particularly cautious.[10] Furthermore, children should not exceed age-appropriate upper limits of nicotinamide intake, as excessive dosages can lead to complications.[10]

Monitoring and Clinical Oversight

Patients receiving nicotinamide should be closely monitored for signs of side effects or interactions with other medications. Regular assessments of liver function and overall health are advisable, especially for those on high-dose regimens or with preexisting health issues.[10][9] As with any supplement, open communication with healthcare providers about all medications and supplements being taken is essential to ensure safety and effectiveness.

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