A Review on the Protective Mechanisms of Taurine in Acute Lung Injury Via the S1P/S1PR1 Signaling Pathway

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Abstract: This review summarises the mechanisms and progress of taurine in alleviating acute lung injury (ALI) by regulating the S1P/S1PR1 signaling pathway. It introduces the biological functions of the S1P/S1PR1 pathway. S1P is a bioactive compound derived from sphingolipid metabolism. By binding to S1PR, it performs various cellular functions and is crucial for regulating vascular barrier function and inflammatory responses. The review also describes the properties of taurine and its protective effects in ALI, including its anti - inflammatory, antioxidant features, and the protection of alveolar epithelial barriers. Emphasis is placed on the interaction between taurine and the S1P/S1PR1 pathway, such as how taurine regulates SphK1/S1P synthesis through its antioxidant capacity and produces a synergistic effect with S1PR1 activators. Finally, future research directions are proposed, including the elucidation of molecular mechanisms, optimisation of dosing regimens, development of combination therapies, and validation of clinical translation. The aim is to provide new strategies for the treatment of ALI.

Keywords: Acute Lung Injury; Taurine; S1P/S1PR1 Signaling Pathway.

1. Introduction

Acute lung injury (ALI), caused by various factors such as infections or trauma, is characterised by alveolar epithelial barrier disruption, neutrophil infiltration, and oxidative stress imbalance. Current clinical treatment mainly relies on mechanical ventilation, yet the mortality rate remains high. In recent years, taurine, a nutritional additive with anti - inflammatory and antioxidant properties, has shown potential in the prevention and treatment of ALI. Furthermore, the signaling pathway mediated by sphingosine - 1 - phosphate (S1P) and its receptor S1PR1 has been proven to regulate pulmonary vascular barrier function and inflammatory responses. This article provides a systematic review of the mechanisms and progress of taurine in alleviating ALI through the modulation of the S1P/S1PR1 pathway.

2. Biological Characteristics of the S1P/S1PR1 Signaling Pathway

S1P, a bioactive compound generated during sphingolipid metabolism, plays a role in promoting cell proliferation, migration, and apoptosis. It is particularly important as an agonist induced in cases of increased vascular leakage and is considered a key phospholipid in regulating angiogenesis and vascular regeneration. Studies have shown that S1P is primarily transported outside the cell membrane via endocrine or paracrine pathways. By binding to S1P receptors (S1PRs) on the cell membrane, it promotes the proliferation of vascular endothelial cells, protects the integrity of endothelial barriers, and maintains vascular permeability. As extracellular ligands, S1PRs interact with specific G - protein - coupled receptors. To date, five types of S1PRs (S1PR1–S1PR5) have been identified. They belong to the family of phospholipid signaling molecules in G proteins and the endothelial differentiation gene family. Among these, S1PR1 is widely distributed in mammals and plays a key role in the formation, proliferation, and migration of vascular endothelial cells by specifically binding to S1P. In lipopolysaccharide (LPS) - induced ALI mouse models, S1P has been shown to significantly reduce pulmonary vascular leakage and inflammatory responses. Extensive research indicates that the regulation of the S1P/S1PR1 signaling pathway in pulmonary endothelial cells plays an important role in lung injury. For

instance, hyperoxia - induced p47 phox activation and reactive oxygen species (ROS) production are mediated by the S1P transporter Spns2 and the S1P/S1PR1 and S1PR2 signaling axes in pulmonary vascular endothelial cells. Additionally, the binding of S1P to S1PR1 can limit excessive inflammatory responses and inhibit the activation of the NLRP3 inflammasome and nuclear factor - κB (NF - κB). During COVID - 19 infection, this mechanism protects pulmonary vascular endothelial cells and exerts anti - inflammatory effects.

3. Protective Effects of Taurine in ALI

3.1 Properties of Taurine

Taurine was first discovered in 1827 as a component of bovine bile. It is a sulfonic amino acid available in mammals. Due to the sulfonate group at the C - terminus, it is systematically named as 2 - aminoethanesulfonic acid. Also, because it has an amino group on the β - carbon, it is also known as β - sulfonic amino acid. With a chemical formula of H2N - CH2 - CH2 - SO3H, it is relatively stable. It has a molecular weight of 125.15, a melting point of 305.11 °C, and begins to decompose at 317 °C. Taurine is usually a colourless, odourless, slightly acidic tetragonal needle - like crystal or powder. It is water - soluble but not soluble in ethanol, ether, or acetone. As a cysteine derivative, it not only participates in growth and metabolism but also helps maintain immune functions. It exerts crucial physiological effects on all body cells, such as endogenous antioxidant, detoxification, anti - inflammatory, and membrane - stabilising actions. As a potential pharmacologically active substance, it can prevent and treat various diseases and conditions across different organ systems, including skin, cardiovascular, respiratory, muscular, skeletal, circulatory, and endocrine systems.

3.2 Anti - Inflammatory Effects of Taurine in ALI

Inflammation is a physiological response of the body to various pathological injuries and stimuli. Uncontrolled pulmonary or systemic inflammation is a major mechanism of ALI/ARDS. Smoke inhalation can trigger strong and complex inflammatory responses in the airway mucosa and lung parenchyma, leading to mucosal damage and ultimately resulting in pulmonary oedema and ventilation - perfusion mismatch. During this process, various cells, including polymorphonuclear neutrophils, macrophages, vascular endothelial cells, alveolar epithelial cells, and fibroblasts, respond to lung injury by activating inflammatory and immune responses. Inflammatory factors induced by alveolar damage can destroy alveolar epithelial cells, increase epithelial permeability, and disrupt vascular integrity.

4. Interactions Between Taurine and the S1P/S1PR1 Pathway

4.1 Regulation of SphK1/S1P Synthesis

Taurine may regulate the activity of sphingosine kinase 1 (SphK1) and the generation of S1P through multiple mechanisms. Its potent antioxidant ability can inhibit the oxidative modification and inactivation of SphK1, thereby maintaining S1P homeostasis. Similar to forsythoside (KD-1), taurine enhances S1P biosynthesis by upregulating SphK1 expression, significantly alleviating alveolar edema and neutrophil infiltration in an influenza virus pneumonia model. Taurine may also provide energy substrates for SphK1 catalysis by regulating ATP levels.

4.2 Synergistic Activation of the S1PR1 Signaling Pathway

Taurine and S1PR1 activators exhibit synergistic effects in several ways. In terms of barrier repair, taurine reduces pulmonary vascular permeability, complementing the reconstruction of endothelial tight junctions mediated by S1PR1. In terms of inflammation suppression, both target the NF - κB pathway. Taurine inhibits the degradation of IκBα, while S1PR1 blocks the activation of the IKK complex to regulate inflammatory responses. In terms of redox balance, taurine directly scavenges ROS, and S1PR1 upregulates the expression of antioxidant genes, achieving dual - layer regulation.

5. Future Research Directions

Future research should focus on several key directions. First, there is a need to clarify the molecular mechanisms of how taurine modulates the SphK1/S1P/S1PR1 pathway in ALI. Second, the optimisation of taurine administration protocols is crucial. Since most

current studies focus on preventive dosing, it is essential to explore therapeutic windows and dose - response relationships to determine the optimal taurine concentration for different stages of ALI. Third, the development of combination therapies should be pursued. Synergistic treatment plans using taurine and S1PR1 agonists should be created, and multi - omics technologies should be employed to assess their combined effects on endothelial barrier repair and inflammation suppression. Finally, clinical translation efforts should be advanced. The preventive use of taurine in high - risk ALI populations, such as those with sepsis or trauma, should be investigated. Dynamic monitoring of clinical efficacy and safety using biomarkers is also necessary. By modulating multiple targets in the S1P/S1PR1 pathway, taurine offers comprehensive benefits of antioxidation, anti - inflammation, and barrier protection in the prevention and treatment of ALI. In - depth studies of its molecular mechanisms and the promotion of clinical translation could provide a new therapeutic strategy for ALI that is both safe and effective.

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