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纳豆激酶及其药理学研究进展

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摘　要

纳豆激酶是一种源自日本传统发酵食品纳豆的丝氨酸蛋白酶，具有多种生物学活性和药理作用。因其具有强大的溶解血栓的能力，受到广大研究者的关注，有望成为新一代溶栓药物。本文首先介绍了纳豆激酶的来源、提取方法和生物学活性，包括其对特定蛋白质的分解能力和在生物体内发挥的溶栓作用。接着，文章详细讨论了纳豆激酶的多种药理作用，包括其在溶栓、抗炎、神经保护、抗动脉粥样硬化以及改善视网膜健康等方面的潜在应用。此外，文章还展望了纳豆激酶未来的研究方向，强调了继续探索和优化提取纯化方法的重要性，并指出深入了解其分子作用机制对于开发更有效的治疗策略至关重要。

关键词

纳豆激酶，溶栓，药理作用，研究进展

Research Progress in Nattokinase and Its Pharmacology

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Abstract

Nattokinase is a serine protease derived from natto, a traditional fermented food in Japan, which has a variety of biological activities and pharmacological effects. Because of its strong ability to dissolve thrombus, it has attracted the attention of researchers and is expected to become a new generation of thrombolytic drugs. This paper first introduces the source, extraction method and biological activity of nattokinase, including its ability to decompose specific proteins and throm-

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bolytic effect in vivo. Then, the article discussed in detail the various pharmacological effects of nattokinase, including its potential applications in thrombolysis, anti-inflammatory, neuroprotection, anti atherosclerosis and improving retinal health. In addition, the future research directions of nattokinase were also prospected, the importance of continuous exploration and optimization of extraction and purification methods was emphasized, and it was pointed out that in-depth understanding of its molecular mechanism of action was essential to develop more effective therapeutic strategies.

Keywords

Nattokinase, Thrombolysis, Pharmacology, Research Progress

1. 引言

在现代医学和生物科学的领域中，纳豆激酶作为一种独特的生物活性物质，吸引了全球研究者的关注。这种特殊的酶源自日本传统发酵食品纳豆，其独特的药理作用在多个健康领域显示出巨大的潜力。纳豆激酶不仅在传统的日本饮食文化中占有重要地位，同时也在现代医学研究中展现出其多方面的药理效益，在临床和实验研究中均有报道，尤其是在心血管健康、抗炎作用以及神经保护等方面[1] [2] [3]。本文旨在探讨纳豆激酶的生化特性、药理作用及其未来的研究方向。首先，我们将深入探讨纳豆激酶的来源、提取方法及其分子结构与活性。了解这些基础信息对于进一步揭示其作用机制至关重要。接下来，我们将详细分析纳豆激酶的多种药理作用，包括其在溶栓[4]、抗炎[5]、神经保护[6]、抗动脉粥样硬化[7]以及改善视网膜健康方面[8]的应用潜力。

2. 纳豆激酶简介

2.1. 纳豆激酶的来源和提取方法

纳豆激酶最初是从日本的传统发酵食品“纳豆”中发现的。纳豆是一种由大豆经过特定菌种，即巴氏芽孢杆菌(*Bacillus subtilis*)发酵而成的产品[9]。在这个发酵过程中，巴氏芽孢杆菌分泌多种酶类，其中包括纳豆激酶。这种酶因其独特的生化特性和潜在的健康益处而受到重视。随着对纳豆激酶研究的深入，研究者们开始通过现代生物技术，如基因克隆和重组 DNA 技术，来提高纳豆激酶的产量和纯度[10] [11] [12] [13]。纳豆激酶的提取是一个精密且技术要求较高的过程。传统的提取方法涉及将纳豆与特定的溶剂混合，然后通过离心和过滤过程来分离出纳豆激酶[14]。随着技术的发展，现代的提取方法更加高效和精确。例如，使用分子筛选技术、层析技术和电泳技术来提纯纳豆激酶，最高可得到 56.1 倍纯度和 61.9 倍酶活性的纳豆激酶[15] [16] [17] [18]。这些方法不仅提高了提取效率，而且也有助于减少纯化过程中可能出现的污染和酶活性的损失。

2.2. 纳豆激酶的生物学活性

纳豆激酶是一种丝氨酸蛋白酶，属于酶类中的一种。作为一种丝氨酸蛋白酶，纳豆激酶的活性中心包含有特定的丝氨酸残基，这是其催化机制的关键。纳豆激酶的分子量约为 27 kDa，由 275 个氨基酸残

基组成。纳豆激酶的活性受多种因素影响，包括 pH 值、温度、金属离子和抑制剂。研究表明，纳豆激酶在中性或略碱性条件下活性最高，而在酸性环境下活性降低[19]。此外，温度对纳豆激酶的活性也有显著影响，其最佳活性温度通常在 45℃左右[20]。金属离子，如钙和镁，可以增强纳豆激酶的稳定性和活性。而某些重金属离子和化学抑制剂则可能抑制其活性[21]。纳豆激酶的活性主要体现在其对特定蛋白质的分解能力上。它能够特异性地识别并分解纤维蛋白，从而在生物体内发挥溶栓作用。除此之外，纳豆激酶还显示出对其他生物分子的作用，如影响炎症反应的途径和促进神经保护的机制。这种多样的生物学活性使得纳豆激酶成为心血管疾病、神经退行性疾病以及其他健康问题的潜在治疗目标[22]。

3. 纳豆激酶的药理作用

3.1. 溶栓作用

纳豆激酶在医学领域的一个重要应用是其溶栓作用，这一作用对心血管健康具有显著的影响。纳豆激酶的主要作用机制是分解血液中的纤维蛋白，这是血栓形成的关键成分[23]。通过分解纤维蛋白，纳豆激酶能够溶解已形成的血栓，从而恢复正常的血液流动。研究表明，纳豆激酶能够有效降低血液粘稠度，改善血液流动性，这种作用不仅有助于预防血栓形成，还对已经形成的血栓有疗效，尤其是在心脏病和中风的治疗中显示出潜在的应用价值[24] [25]。多项临床研究已经显示，纳豆激酶在溶解血栓方面具有潜在的效果。这些研究通常聚焦于纳豆激酶对心血管疾病患者的影响，特别是对那些有血栓形成风险的患者。纳豆激酶作为一种自然来源的溶栓剂，相比传统药物具有更少的副作用，这使得其在临床应用中具有优势。

3.2. 抗炎作用

除了溶栓作用，纳豆激酶还显示出显著的抗炎活性，这对于治疗各种炎症相关疾病具有重要意义。纳豆激酶的抗炎作用主要通过调节体内的炎症反应途径来实现[26]。这种酶能够影响炎症介质的产生和释放，如降低促炎细胞因子的水平，并增强抗炎介质的表达[27]。通过这种方式，纳豆激酶有助于减轻组织的炎症反应，降低由炎症引起的组织损伤和疼痛。实验研究已经表明，纳豆激酶在动物模型中能有效减少炎症反应。例如，在实验性关节炎的动物模型中，纳豆激酶的应用显著减轻了关节的炎症和肿胀[28]。此外，纳豆激酶也在一些人类临床试验中显示出抗炎效果，尽管这方面的数据还不充分，需要更多的研究来证实[29]。鉴于其抗炎作用，纳豆激酶有望作为一种新的抗炎治疗策略，特别是在治疗慢性炎症疾病如关节炎和自身免疫疾病方面。与传统的非甾体抗炎药物相比，纳豆激酶的自然来源和较低的副作用概率使其成为一个有吸引力的替代选择。

3.3. 神经保护作用

纳豆激酶在神经保护领域的作用是其另一项引人注目的药理特性，它为治疗神经退行性疾病提供了新的可能性。纳豆激酶在神经系统中展现出保护神经细胞免受损害的能力[30]。这一作用机制涉及多种生物学途径，包括抗氧化作用、抑制神经炎症反应以及促进神经细胞生长和再生。纳豆激酶通过这些机制，有助于减少神经退行性疾病中常见的氧化应激和细胞损伤。在实验室研究中，纳豆激酶显示出在多种神经退行性模型中的保护效果，例如阿尔茨海默病和帕金森病模型[31] [32] [33]。这些研究指出，纳豆激酶能够减缓神经退行性过程，并提高神经细胞的存活率。尽管这些研究为纳豆激酶在神经保护方面的应用提供了基础，但人类临床试验的数据还相对有限。未来的研究将重点关注纳豆激酶在神经保护作用的确切机制，以及如何通过临床试验验证其效果。此外，研究还应探索纳豆激酶与现有神经退行性疾病治疗方法的协同作用，以及其长期应用的安全性和有效性。

3.4. 抗动脉粥样硬化作用

动脉粥样硬化是一种常见的心血管疾病，其特征是动脉壁内脂质和纤维组织的积累，导致血管硬化和狭窄。纳豆激酶通过多种机制参与抗动脉粥样硬化的过程。首先，它能够减少血管内脂质的积累，特别是低密度脂蛋白(LDL)的氧化形式，从而减缓动脉壁的炎症和硬化过程[34]。通过降低血液中有害脂质的浓度，纳豆激酶有助于减少心血管疾病的风险。此外，纳豆激酶可同时提高高密度脂蛋白(HDL)的水平，这一作用有助于减少动脉内壁的脂质沉积，从而减缓动脉粥样硬化的发展[35]。动物实验和初步的人类临床研究已经显示了纳豆激酶在抗动脉粥样硬化和降低血脂方面的潜在效果[36]。然而，更广泛和深入的研究仍然需要进行，以更好地理解其作用机制和优化其临床应用。

3.5. 改善视网膜作用

纳豆激酶在眼科学领域也显示出潜在的应用价值，尤其是在改善视网膜健康方面。视网膜是眼睛中的关键组成部分，负责捕捉光线并转换为神经信号，视网膜的健康依赖于良好的血液供应。首先，纳豆激酶的抗氧化作用在保护视网膜健康方面发挥着重要作用。氧化应激是导致视网膜细胞损伤的主要因素之一，尤其是在糖尿病视网膜病变[37]等疾病中。纳豆激酶通过其抗氧化特性，能够减少自由基的产生，保护视网膜细胞免受氧化损伤。这一作用有助于减缓视网膜病变的进展，保持视网膜细胞的功能和结构完整。其次，纳豆激酶在改善眼部血流方面的作用也不容忽视。良好的血液循环对于维持视网膜细胞的健康至关重要，因为血液为视网膜提供必需的氧气和营养物质，纳豆激酶通过其溶栓活性，能够改善眼部血液循环，增加视网膜的血液供应[38]。这些作用有助于减少视网膜疾病如黄斑变性和视网膜血管疾病的风险[39]。这些初步研究为纳豆激酶在眼科疾病治疗中的应用提供了基础。视网膜疾病的治疗通常复杂且难以管理。纳豆激酶作为一种潜在的治疗选项，可能为预防和治疗视网膜疾病提供新的途径。特别是对于那些因血液循环问题或氧化应激引起的视网膜疾病，纳豆激酶的应用可能带来积极的影响。

4. 展望

为了更高效地利用纳豆激酶的药理特性，研究者将继续探索和优化其提取和纯化方法。通过使用先进的生物技术和工程手段，可以提高纳豆激酶的产量和纯度，从而降低成本并提高其在医药产品中的可用性。尽管纳豆激酶的多种药理作用已被初步揭示，但其具体的分子作用机制仍需进一步研究。通过深入了解其与人体细胞和分子之间的相互作用，可以为开发更有效的治疗策略提供科学依据。纳豆激酶的研究涉及多个学科领域，包括生物化学、分子生物学、药理学和临床医学。未来的发展将依赖于这些领域之间的紧密合作，以及与制药工业的协同努力，共同推动纳豆激酶的研究和应用。

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