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Hans汉斯

壳聚糖基水凝胶在皮肤创口修复中的应用研究

马　馨[1]，张孟宇[1]，宋佳栩[1]，潘晓萱[2]，唐　艳[3*]，王晓敏[3*]

[1]青岛大学青岛医学院，山东　青岛
[2]黑龙江中医药大学第二临床医学院，黑龙江　哈尔滨
[3]青岛大学再生医学与检验创新研究院，山东　青岛

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摘　要

壳聚糖作为一种天然线性多糖，拥有许多独特的性质，这些性质使得其成为生物医学领域重点研究的对象。首先，壳聚糖具有一定的生物活性，这种性质能够促进细胞增殖和组织修复，对于加速创口愈合具有重要意义。其次，壳聚糖还有优越的抗菌能力，能抑制多种细菌的生长，有效防止创口感染。而使壳聚糖基水凝胶能够安全可靠地应用于人体的，则是壳聚糖良好的生物相容性，这种性质能有效减少人体的免疫反应及毒性反应。使用壳聚糖制成的壳聚糖基水凝胶，除了拥有上述壳聚糖的性质外，还拥有高吸水性、柔软性和可变形性等多种性质。其中，高吸水性使得创口环境能够保持湿润，有助于促进创口愈合；柔软性让其能够紧密贴合创面，为创口提供良好保护；可变形性则通过改变水凝胶的自身形状，在创口修复中更好地模拟人体皮肤，从而促进组织的再生和修复。这种性质使得壳聚糖基水凝胶成为制作皮肤创口敷料的理想材料，在多种类型的皮肤创伤修复中，表现出了显著的优越性。

关键词

壳聚糖，水凝胶，皮肤创口，修复机制，修复效果

Study on the Application of Chitosan-Based Hydrogels in Skin Wound Repair

Xin Ma[1], Mengyu Zhang[1], Jiaxu Song[1], Xiaoxuan Pan[2], Yan Tang[3*], Xiaomin Wang[3*]

[1]Qingdao Medical College, Qingdao University, Qingdao Shandong
[2]The Second Clinical Medical College of Heilongjiang University of Chinese Medicine, Harbin Heilongjiang
[3]Institute of Regenerative Medicine and Laboratory Innovation, Qingdao University, Qingdao Shandong

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*通讯作者。

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Abstract

As a natural linear polysaccharide, chitosan has many unique properties, which make it the focus of biomedical research. Firstly, chitosan has certain biological activity, which can promote cell proliferation and tissue repair, and is of great significance for accelerating wound healing. Secondly, chitosan has superior antibacterial ability, which can inhibit the growth of a variety of bacteria and effectively prevent wound infection. What makes chitosan-based hydrogels safe and reliable to be applied to human body is the good biocompatibility of chitosan, which can effectively reduce the immune reaction and toxic reaction of human body. The chitosan-based hydrogels made of chitosan have many properties, such as high water absorption, softness and deformability, in addition to the properties of chitosan mentioned above. Among them, high water absorption keeps the wound environment moist, which helps to promote wound healing; The softness makes it fit tightly to the wound, providing good protection for the wound; Deformability can better simulate human skin in wound repair by changing the hydrogel's own shape, thus promoting tissue regeneration and repair. This kind of property makes chitosan-based hydrogels an ideal material for making skin wound dressings, showing remarkable superiority in many types of skin wound repair.

Keywords

Chitosan, Hydrogel, Skin Wound, Repair Mechanism, Repair Effect

1. 引言

针对皮肤创口的修复是生物医学领域的重点研究方向，但传统疗法存在多方面的严重局限性。壳聚糖作为一种天然多糖，在具有促进组织修复的能力的同时，还有优异的抗菌性和生物相容性[1] [2]。而水凝胶因其高吸水性、柔软性和可变形性，在皮肤创口修复中展现出巨大潜力[3]。以壳聚糖为材料制成的壳聚糖基水凝胶，不仅能保留壳聚糖的促进组织修复的能力，还拥有水凝胶的高吸水性和柔软性，为创口愈合提供一个湿润的环境。除了修复创口时在多个方面的显著优势，这种材料在临床应用中极富竞争力的原因还在于能够适用于多种类型的皮肤创伤。研究表明，壳聚糖基水凝胶在皮肤创口修复中具有广阔的应用前景，对这种新材料的探索为开发新型创口敷料提供了重要的理论依据和实践指导[4]。现综述了近年来将壳聚糖基水凝胶应用于皮肤创口修复中的研究，深入探讨壳聚糖基水凝胶的促进组织再生和抗菌抗炎等特性，分析其在不同类型皮肤创伤中的修复效果和作用机制，以期为推动壳聚糖基水凝胶在皮肤创口修复领域的临床应用和发展提供理论依据。

2. 壳聚糖基水凝胶在皮肤创口修复中的优势

2.1. 促进组织再生

壳聚糖基水凝胶具有促进组织快速再生的能力，通过激活成纤维细胞的增殖迁移，胶原蛋白的合成速度加快，组织得以再生[5] [6]。研究表明，在感染创口模型中，壳聚糖基水凝胶显著提高了胶原蛋白的沉积量，并优化了胶原蛋白的排列，使新生组织更接近正常皮肤结构。同时，通过释放血管内皮生长因子(VEGF)促进内皮细胞增殖，壳聚糖基水凝胶能显著提升创口处血管的生成能力[7] [8]。而在皮肤溃疡

模型中，壳聚糖基水凝胶也表现出了良好的修复作用[9]，能够通过促进胶原蛋白沉积和血管生成，加速溃疡创口的愈合[10]。例如，在全层皮肤创口模型中，一种基于壳聚糖和甲基纤维素的温敏型水凝胶(CSDA-MC-HG)表现优异，在修复创口的过程中能够有效促进成纤维细胞的增殖和新血管的形成[11]。因此，创口处的血管能够快速重生，提供充足的氧气和营养物质，从而加快创口处组织的再生和修复[12]。在烧伤创口中，壳聚糖基水凝胶拥有的促进组织再生的能力，能够显著加快创口的愈合[13]。例如，基于壳聚糖/海藻酸盐的水凝胶，加载上血管内皮钙黏蛋白(VE-cadherin)和成纤维细胞生长因子(FGF)，能够在不同程度的皮肤烧伤模型中显著提高组织修复能力[14]。实验结果显示，这种水凝胶在约 24 天内就能实现深度烧伤创口的实质性修复。在慢性创口的修复过程中，壳聚糖基水凝胶也能加快组织再生，表现出显著的促进作用。例如，一种基于羧甲基壳聚糖的水凝胶(CMCS-TA/Cu^{2+})，通过加载单宁酸/铜离子(TA/Cu^{2+})纳米颗粒，能够持续释放铜离子，从而促进细胞迁移和管状结构的形成，最后达到加快慢性创口愈合的结果。实验结果显示，这种水凝胶在 9 天内能够达到 90%以上的创口修复率，在多种修复材料中表现优异[15]。

2.2. 抗菌作用

壳聚糖具有天然的抗菌特性，其抗菌机制主要通过壳聚糖分子链上的氨基与细菌细胞壁上负电荷的相互作用，来破坏细菌细胞膜的完整性，从而抑制细菌生长[16] [17]。而在壳聚糖基水凝胶中，壳聚糖的抗菌性得以保留并进一步增强，与此同时，该材料还具有高吸水性和三维网络结构，能够有效吸附创口渗出液，进一步减少细菌的滋生环境[18] [19]。这种高吸水性和柔软性也能帮助其更好地贴合创面，为伤口提供一个湿润的愈合环境，加速创口愈合[20] [21]。并且对多种细菌(如耐甲氧西林金黄色葡萄球菌和大肠杆菌)，壳聚糖基水凝胶都具有显著的抗菌效果，尤其在近红外光照射下，抗菌性能将得到进一步增强[22]。多方机制共同带来的抗菌能力不仅可以有效预防创口感染，还有加速创口愈合的效果。而在实际应用方面，壳聚糖基水凝胶在生物相容性和抗菌性方面具有极大优势，使其与传统敷料相比，能够有效减少创口感染的风险[23] [24]。

2.3. 抗炎作用

壳聚糖通过调节免疫反应，抑制炎症因子(如 TNF-α 和 IFN-γ)表达，以及促进抗炎因子(如 IL-4 和 TGF-β1)分泌等多种手段，可以有效降低创口处炎症的反应。而壳聚糖调节机体免疫反应，具体为壳聚糖能够与炎症细胞相互作用，调节其功能和代谢，从而抑制炎症因子的表达，有效减轻创口处的炎症反应[25]。这使得壳聚糖基水凝胶在临床应用上，尤其是在治疗慢性溃疡和复杂创口方面具有显著优势。而使用壳聚糖制成的壳聚糖基水凝胶，既保留了壳聚糖的这种抗炎特性，又能形成一种湿润的物理屏障，从而能够进一步隔离炎症诱导因子，保护创口免受病原体侵害[26] [27]。通过其高含水量和可变形性，壳聚糖基水凝胶可作为阻挡炎症因子的有效屏障，减少炎症介质的扩散，同时还能吸收创口渗出液，维持局部微环境的稳定[20] [28]。与此同时，在慢性创口中，由于其拥有的抗氧化性和抗炎特性，壳聚糖基水凝胶能有效减轻创口周围的炎症反应。研究表明，CMCS-TA/Cu^{2+}水凝胶能够显著降低自由基的产生，减少氧化应激对创口的影响，同时促进胶原蛋白的积累和再生。这种机制使壳聚糖基水凝胶在慢性创口的修复中展现了良好的抗炎效果，也具有促进愈合的能力[15]。这种多维度的抗炎作用除了能够促进创口从炎症期向增殖期的顺利转变外，也能进一步促进组织修复。

综上所述，壳聚糖基水凝胶在皮肤创口修复中展现出显著的促进组织再生和抗菌抗炎能力，为创口愈合提供了理想的微环境，并且在不同类型的皮肤创伤中均表现出优越的修复效果，在临床应用上具有广阔的前景和极高的应用价值[29]。

3. 壳聚糖基水凝胶的具体作用机制

壳聚糖基水凝胶在实际作用过程中的修复效果由多种因素综合决定，其中起到关键作用的有水凝胶的交联方式、壳聚糖溶液浓度和壳聚糖的分子量。

3.1. 交联方式

交联方式是影响壳聚糖基水凝胶修复效果的关键因素之一，包括化学交联和物理交联。化学交联，例如使用戊二醛、京尼平等交联剂，可以形成长效稳定的三维网络结构，延长药物缓释周期，尤其适用于深度创面修复[30]；而物理交联(如离子交联、温敏交联)则能够快速适应创口渗出液环境，形成动态可逆的凝胶层，以促进急性创面的初期炎症调控[31] [32]。

3.2. 壳聚糖溶液浓度

不同浓度的壳聚糖溶液制备的水凝胶在微观结构与生物反应上存在显著差异[33]。当壳聚糖浓度较低时，水凝胶的孔隙率较高，这有利于成纤维细胞的深层渗透和血管内皮细胞的迁移，但相应地会导致水凝胶机械强度不足[34]；而浓度较高时，水凝胶会形成更加紧密的三维网络结构[35]，虽然更高的机械强度使药物在其内部的扩散速度相对较慢，但也因此让其具有更持久的药物缓释能力，从而使药物在创口处能更长时间地维持有效浓度，延长治疗效果。这种壳聚糖溶液浓度变化带来的不同修复效果，使壳聚糖基水凝胶能通过精准调控浓度参数，实现从急性创面的抗菌消炎到慢性创面的组织再生的全周期治疗功能[36]。

3.3. 分子量

高分子量的壳聚糖通常具有更好的机械性能[37]。在制备水凝胶时，高分子量壳聚糖形成的网络结构更加稳定，能够承受更大的外力，这在修复承重组织或易受摩擦的创口时具有显著优势。但是，高分子量壳聚糖的溶解性相对较差，在制备时需要使用特殊工艺以保证高分子壳聚糖能均匀分散。而低分子量壳聚糖则拥有更好的生物活性，细胞表面受体的相互作用更强，能够更有效地促进细胞的黏附、增殖和分化，这有利于组织的修复和再生[38]。

4. 结论

壳聚糖基水凝胶在皮肤创口修复中展现了显著的潜力和优势[39]。通过壳聚糖的独特性质，运用多种机制，有效实现促进组织再生及抗菌抗炎作用。针对不同的皮肤创伤，壳聚糖基水凝胶也均表现出良好的修复效果。对于烧伤创口，它能加速愈合，与其他治疗方法相比，具有更好的生物相容性和抗菌性能；在皮肤溃疡治疗中，促进胶原蛋白沉积和血管生成，展现出广阔的临床应用前景；对于慢性创口，其抗氧化和抗炎特性有效减轻炎症反应，促进创口愈合。

为了进一步提高壳聚糖基水凝胶的性能，未来的研究可进一步聚焦于新型交联剂和复合材料的应用。例如，壳聚糖基水凝胶通过与纳米材料(如纳米银、氧化锌等)的结合，可以进一步增强其抗菌性能[40]。此外，其与生物活性因子(如生长因子、细胞外基质蛋白等)的结合，可以进一步促进创口的组织再生和修复。对新型复合材料的深入探索，能为壳聚糖基水凝胶在创口修复中的应用提供更广阔的可能性[41]。

而要想在临床中使用壳聚糖基水凝胶，需要进行严格的安全性评估[42]。尽管壳聚糖本身具有良好的生物相容性，但其化学修饰后的衍生物仍可能引发潜在的免疫反应或毒性问题。因此，在将壳聚糖基水凝胶投入临床应用前，需要进行大量的体内外实验和临床试验，验证其在复杂创口环境中的安全性和稳定性。同时需要兼顾包括生产工艺的复杂性、成本控制以及与现有医疗体系的兼容性等一系列问题。为

解决这些问题，可以加强产学研合作，优化生产工艺，降低生产成本，并通过多学科交叉研究，推动壳聚糖基水凝胶在临床中的广泛应用[43]。

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