

论著·基础研究

高亲水性静电纺丝短纤维海绵促创面愈合的作用

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[摘要] **目的**·构建一种含有氧化石墨烯(graphene oxide, GO)的高亲水性静电纺丝短纤维海绵(Sponge@GO), 探究其对慢性创面的促愈合作用。**方法**·分别将不含及含有GO的纺丝液经过纺丝成膜、打碎、塑形并用戊二醛交联后, 制备出2种短纤维海绵(Sponge和Sponge@GO)。采用扫描电子显微镜(scanning electron microscope, SEM)观察2种海绵的内部结构, 通过接触角及吸水率观察两者的亲水性能。经CCK-8法和活/死细胞染色验证海绵的生物相容性。将12只6周龄SD雄性大鼠分为对照组、Sponge组和Sponge@GO组, 每组各4只; 通过腹腔注射1%的链脲佐菌素溶液建立糖尿病模型, 建模后每只大鼠背部制备3块直径1.0 cm的全层皮肤缺损; 将材料覆盖于创面, 使用医用纱布覆盖创面并固定(对照组仅覆盖无菌纱布包扎); 分别于术后第7、14日测量并计算创面愈合率, 同时取创周0.5 cm内组织行苏木精-伊红染色(hematoxylin and eosin staining, H-E染色)、Masson染色观察病理学改变; 并在第14日通过 α -平滑肌肌动蛋白(α -smooth muscle actin, α -SMA)免疫荧光染色, 观察血管形成情况。**结果**·SEM观察显示, 与Sponge海绵比较, Sponge@GO海绵的纤维直径较细, 孔隙率偏大。2种短纤维海绵在10 min内均基本达到最大吸水率, Sponge@GO海绵的吸水率较高。Sponge@GO海绵的接触角小于Sponge海绵, 差异有统计学意义($P=0.000$)。CCK-8法检测结果显示, 术后第3、5日Sponge组与对照组相比, 尚呈现出细胞增殖的状态(均 $P<0.05$), 而Sponge@GO组与对照组的差异无统计学意义。活/死细胞染色结果显示, 3组细胞均呈现良好的增长态势。SEM和荧光染色观察显示, Sponge@GO海绵内部的细胞数量明显较Sponge海绵多。3组大鼠的创面均未见感染。Sponge@GO组和Sponge组术后第7日的创面愈合率均显著高于对照组(均 $P<0.05$); 第14日, Sponge@GO组的创面愈合率仍显著高于对照组($P=0.009$), 而Sponge组与对照组之间的差异无统计学意义。术后第14日, H-E染色显示Sponge@GO组创面肉芽组织更加成熟, 结构更为均匀致密; Masson染色显示Sponge@GO组胶原更加致密, 上皮化显著; α -SMA免疫荧光染色显示Sponge@GO组新生血管数量更多, 密度更高。**结论**·Sponge@GO海绵在吸收渗液后可维持创面微湿润环境, 有利于促进伤口愈合。

[关键词] 氧化石墨烯; 短纤维; 静电纺丝; 创面修复**[DOI]** 10.3969/j.issn.1674-8115.2023.03.002 **[中图分类号]** R641 **[文献标志码]** A

Effect of high hydrophilic electrospun short fibrous sponge on wound repair

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[Abstract] **Objective**·To construct an electrospun short fibrous sponge (Sponge@GO) laden with graphene oxide (GO) for chronic wound healing. **Methods**·Two types of short fibrous sponges (Sponge and Sponge@GO) without and with GO were prepared by means of electrospinning, homogenizing, shaping and crosslinking with glutaraldehyde, respectively. The internal structures of the two sponges were observed with a scanning electron microscope (SEM), and their hydrophilic properties were observed via contact angle and water absorption rate. The biocompatibility of the sponge was verified by CCK-8 and live/dead staining. Twelve 6-week-old SD male rats were divided into control group, Sponge group and Sponge@GO group, with 4 rats in each group. The diabetes models were established by intraperitoneal injection of 1% streptozotocin solution, and three full-layer skin defects with a diameter of 1.0 cm were prepared on the back of each rat after modelling. Covering on the wound, the material was fixed with medical gauze.

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The control group was only covered with sterile gauze dressing. The wound healing rate was measured and calculated on Day 7 and 14, respectively, while hematoxylin-eosin (H-E) staining and Masson staining were performed on tissues within 0.5 cm around the wound to observe pathological changes. The angiogenesis was observed by α -smooth muscle actin (α -SMA) immunofluorescence staining on Day 14. **Results**·SEM observation showed that the fiber diameter of Sponge@GO was significantly thinner and the porosity increased. The two types of short fiber scaffolds basically reached the maximum water uptake within 10 min, but the Sponge@GO scaffold showed better water absorption performance. The water contact angle of Sponge@GO scaffold was significantly smaller than that of Sponge, and the difference was statistically significant ($P=0.000$). The results of CCK-8 method showed that on Day 3 and 5, the Sponge group had better cell proliferation compared with the control group (both $P<0.05$), while there was no statistical significance between Sponge@GO group and control group. The results of live/dead staining showed that all the three groups of cells showed good cell growth trend. SEM and fluorescence staining showed that there were more cells in the Sponge@GO scaffold. *In vivo* experiment, no infection was found on the wound surface of the three groups of rats. The wound healing rate of Sponge@GO and Sponge groups was significantly higher than that of control group on Day 7 (both $P<0.05$). On Day 14, the wound healing rate of the Sponge@GO group was still significantly higher than that of the control group ($P=0.009$), while the difference between the Sponge group and the control group was not statistically significant. On Day 14, H-E staining showed more mature granulation tissue and more uniform and dense structure in the Sponge@GO group; Masson staining showed more dense collagen and significant epithelialization in the Sponge@GO group; α -SMA immunofluorescence staining showed more neovascularization and higher density in the Sponge@GO group. **Conclusion**·Sponge@GO sponge can ensure micro-moist environment on the wound surface after absorbing exudate and has shown promising results in promoting wound healing.

[Key words] graphene oxide (GO); short fiber; electrospinning; wound repair

由糖尿病、动脉硬化性闭塞症、放射治疗等因素导致的创面，通常因血供不足、胶原蛋白生成减少，而无法在预期时间内顺利愈合，从而由急性创面演变为难愈性慢性创面^[1-4]。糖尿病足溃疡 (diabetic foot ulcer, DFU) 作为糖尿病严重并发症之一，患病率及患者截肢率居高不下^[5]。根据国际糖尿病联合会 (International Diabetes Federation, IDF) 的预测^[6]，至 2045 年糖尿病患病率将由 2017 年的 8.4% 升至 9.9%，其中约 1/4 的患者可伴有 DFU^[5,7]。目前，外用敷料仍是促进创面愈合的主要方法之一。虽然渗出液内含有丰富的营养成分，但在慢性创面愈合过程中，由于炎症期较长可致渗出液流出过多，反而造成伤口浸渍、微环境改变，进而再次延缓愈合^[8-9]。传统敷料，例如纱布或者其他棉质材料等，虽然成本低，但易导致伤口快速脱水，需要经常更换；同时，因孔隙过大，肉芽组织易长入孔隙内，造成换药时新生组织的二次损伤^[10-11]。理想的伤口敷料应具备生物相容性好、有一定的亲水性、允许内部气体与外界交换等优势^[12-13]，既可以清除多余渗出液，又可以保留渗液内的活性物质，不仅能为伤口提供微湿润环境，还应有利于细胞的黏附、迁移及血管生成，为周围组织提供氧分及营养物质^[14-15]，最终达到促进伤口愈合的效果。因此，开发一种优良的创面敷料尤为重要。

近年来，由电纺技术与冷冻成形技术相结合制备的三维 (3D) 仿生短纤维海绵支架，无论是比表面积还是孔隙率均优于二维 (2D) 纺丝膜，同时能够为体外细胞的负载及黏附增殖提供生态位^[16-17]。氧

化石墨烯 (graphene oxide, GO) 作为石墨烯的氧化衍生物，不仅可增强材料的吸水能力，进一步增强聚合物的生物相容性及生物活性^[18-19]，还可以明显促进血管生成^[20-21]。基于此，本研究构建了一种负载 GO 的静电纺丝短纤维海绵 (Sponge@GO)，利用 GO 的吸水能力增强该海绵的亲水性，使其在不断吸收渗液的同时，还能保持创面的微湿润环境，提高其在创面的黏附能力，避免造成二次伤害；同时，观察该材料在动物模型创面修复中的应用效果。

1 材料与方 法

1.1 实验材料

明胶 (CAS 9000-70-8, Sigma-Aldrich)，聚乳酸 (polylactic acid, PLA; CAS 26100-51-6, 岱罡生物)，六氟异丙醇 (hexafluoroisopropanol, HFIP; CAS 920-66-1, 九鼎化学)，氧化石墨烯分散液 GO (CAS 7440-44-0, 2 mg/mL, 先丰纳米)，叔丁醇 (CAS 75-65-0, 罗恩)，25% 戊二醛 (CAS 111-30-8, 麦克林)，谷氨酸 (CAS 56-86-0, Aladdin)，高糖培养基 (AH29892317, Cytiva)，胎牛血清 (fetal bovine serum, FBS; 2168090RP, Gibco)，青霉素-链霉素溶液 (penicillin-streptomycin, P/S; 65BA23, Bioagrio)，CCK-8 试剂盒 (112921220303, 碧云天)，活/死细胞试剂盒 (122021220509, 碧云天)，电子显微镜固定液 (G1102, Servicebio)，4% 多聚甲醛 (BL539A, Biosharp)，牛血清蛋白 (bovine serum protein, BSA; CAS 9048-46-8, Aladdin)，Triton X-100 (CAS 9002-

93-1, Aladdin), DAPI染液 (G1012, Servicebio), 鬼笔环肽染色试剂 (G1041, Servicebio), 链脲佐菌素 (streptozotocin, STZ; CAS 18883-66-4, 索莱宝), 水合氯醛 (CAS 302-17-0, 源叶生物)。

1.2 短纤维支架的制备及表征

1.2.1 短纤维支架的制备 将明胶、PLA按4:1的质量比溶解于HFIP中, 配制成浓度为12%的基础纺丝液^[16-17]; 过夜搅拌, 待彻底溶解成乳白色黏稠液体后, 电纺成膜。具体过程: 用10 mL注射器(配备22 G针头)抽取纺丝液后, 固定于注射泵上; 将铝箔纸缠绕于距针头15 cm外的滚轴上, 设置参数(18 kV, 3 mL/h)后, 进行静电纺丝。同样, 在混合均匀的基础纺丝液中加入1 mL GO继续搅拌2 h, 直至纺丝液内无明显颗粒状沉淀且完全溶解后, 用上述步骤将GO纺丝液电纺成膜。

分别将明胶/PLA和明胶/PLA/GO的电纺膜剪碎, 根据2%的密度加入叔丁醇, 使用高速匀浆机(IKA T25, 德国)打碎(转速9 000 r/min), 15 min后得到分散液。将其分装于细胞培养板内, 在-80 °C下冷冻过夜, 放于冷冻干燥机(Gold-SIM)内冻干塑形, 得到未交联的短纤维支架。使用戊二醛溶液(25%戊二醛与无水乙醇按1:4体积比混合)对2种支架进行化学交联以稳固支架的性状。为提高支架的生物相容性, 经去离子水冲洗后, 将支架浸泡于含有5%谷氨酸的0.5 mol/L盐酸溶液中48 h^[22]。去离子水冲洗后冻干成型, 得到不同成分的短纤维支架, 即Sponge和Sponge@GO支架。

1.2.2 短纤维支架的表征 对冻干后的2组支架切取薄层后喷金, 利用扫描电子显微镜(scanning electron microscope, SEM; Hitachi TM-100, 日本)观察内部形貌特征。为了测试支架的亲水性, 通过接触角仪(OCA 40, 德国Datafystics)将去离子水滴于支架表面, 测量接触支架后第5 s时的接触角。取干态下的支架称重, 然后在去离子水中浸泡10、30、60、120 min, 于各时间点取出再次称重。吸水率(%)=(湿重-干重)/干重×100%, 计算各支架的吸水率。

1.3 细胞实验

1.3.1 生物相容性检测

(1) 材料灭菌 将支架置于75%乙醇中浸泡24 h; 随后用磷酸盐缓冲液(phosphate buffer saline,

PBS)浸泡3次, 每次5 min。此过程在超净台中完成, 以保证材料无菌。

(2) 浸提液的制备 将灭菌后的材料按照0.1 g/mL的比例置于培养基中, 放入37 °C、5% CO₂的培养箱中静置3 d后收集培养基, 按10%的体积分数加入FBS并过滤, 得到浸提液。利用浸提液进行材料相容性的检测。

(3) CCK-8法检测细胞毒性 使用CCK-8法测定人脐静脉内皮细胞(human umbilical vein vessel endothelial cells, HUVECs)在Sponge和Sponge@GO浸提液中的细胞毒性。将HUVECs按3 000个/孔的密度种于96孔板中, 待细胞贴壁后分别换成2组支架的浸提液; 对照组使用高糖培养基。随后于换液后的第1、3、5日弃旧培养基, 用PBS冲洗3次后, 各孔加入90 μL高糖培养基和10 μL CCK-8试剂后继续在培养箱内孵育1.5 h。最后使用酶标仪检测450 nm波长下的吸光度。

(4) 活/死细胞染色观察 将HUVECs按20 000个/孔的密度种于24孔板中, 待贴壁后换成各组支架的浸提液培养; 对照组仍用高糖培养基继续培养细胞。分别在换液后的1、3、5日弃旧培养基, 用PBS冲洗3次后, 每孔加入200 μL配制好的活/死细胞染色试剂(5 μL钙黄绿素与5 μL碘化丙啶加入10 mL缓冲液中), 避光孵育30 min后用荧光显微镜观察。

1.3.2 材料黏附性 取无菌支架在高糖培养基中浸泡1 h后, 将HUVECs按30 000个/支架的密度接种于支架上, 期间每2 d更换培养基。培养7 d后, 弃培养基, 用PBS清洗2次。一部分支架使用4%多聚甲醛固定24 h, 每孔加入适量0.2% Triton X-100溶液处理5 min, PBS冲洗3次后加入2% BSA溶液孵育30 min, 加入鬼笔环肽避光孵育30 min, PBS再次冲洗后加入DAPI孵育30 s, PBS清洗后进行荧光显微镜观察并拍照。另一部分支架用电子显微镜固定液在4 °C下固定24 h, 再经梯度乙醇(30%、50%、70%、80%、90%、95%和100%)脱水5 min后, 进行样品冻干, 喷金后进行SEM观察并拍照。

1.4 体内实验

1.4.1 实验动物 选择SPF级6周龄SD雄性大鼠12只, 体质量(200±10) g, 购自上海杰思捷实验动物有限公司。动物生产许可证号为SCXK(沪)2018-0004, 使用许可证号为SYXK(沪)2021-0009。

1.4.2 建模及分组处理 在实验开始前适应性喂养1周, 禁食12 h后按55 mg/kg的剂量腹腔注射1%的STZ溶液(使用0.1 mol/L、pH值4.5的柠檬酸缓冲液配制, 避光冰浴操作)。1周后出现多饮、多食、多尿症状且随机血糖 >16.7 mmol/L即为糖尿病建模成功。将动物随机分成3组(对照组、Sponge组和Sponge@GO组), 每组各4只。建模后腹腔注射水合氯醛(0.4 mL/100 g)进行麻醉, 备皮消毒, 在每只大鼠背部制备3块直径1.0 cm的全层皮肤缺损。将材料覆盖于创面后拍照, 使用医用纱布覆盖创面并固定(对照组仅覆盖无菌纱布包扎)。

1.4.3 创面观察 分别于术后第7、14日打开敷料并拍照(期间视创面情况进行碘伏消毒换药)。使用ImageJ图像软件进行测量, 计算愈合率。愈合率=(原始创面面积-各时间点创面面积)/原始创面面积 $\times 100\%$ 。同时在各时间点取材(创周0.5 cm内组织), 进行苏木精-伊红染色(hematoxylin and eosin staining, H-E染色)、Masson染色, 观察病理学改变。在第14日通过 α -平滑肌肌动蛋白(α -smooth muscle actin, α -SMA)免疫荧光染色观察

血管形成情况。

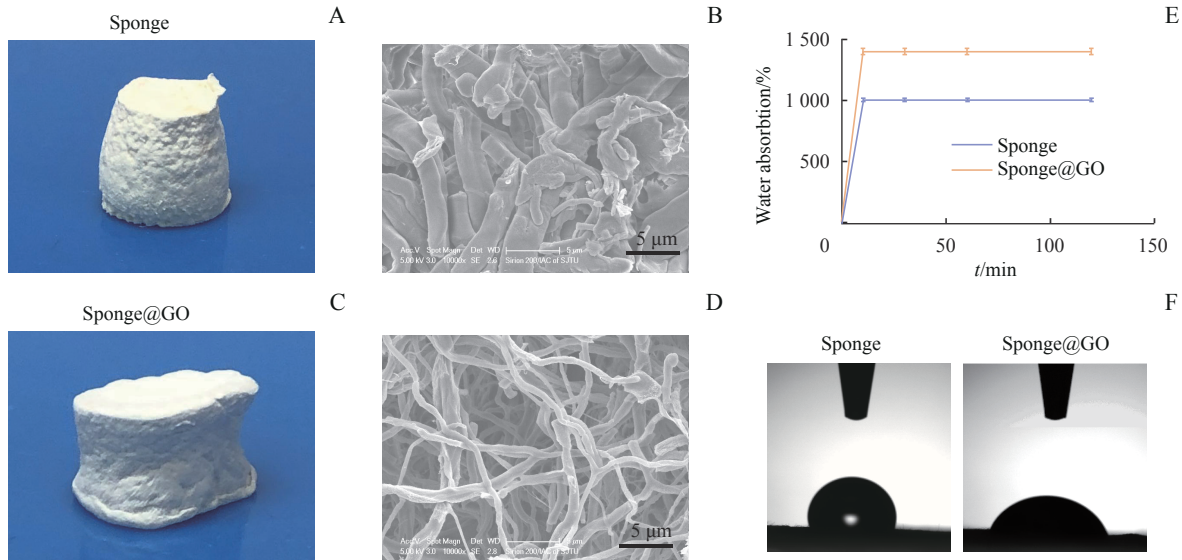
1.5 统计学方法

所有实验数据均通过GraphPad Prism 8.0统计软件进行分析。数据以 $\bar{x}\pm s$ 形式表示, 通过单因素方差分析进行组间比较。 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 支架外观、内部纤维结构和吸湿性能

与Sponge比较, Sponge@GO颜色稍深(图1A、C); SEM观察显示Sponge@GO纤维直径较细, 孔隙率偏大(图1B、D)。2种短纤维支架在10 min内均基本达到最大吸水率(图1E), Sponge的吸水率可达(1 007.82 \pm 14.54)%, Sponge@GO的吸水率可达(1 401.92 \pm 24.81)%。Sponge支架的接触角为104.98 $^{\circ}\pm$ 4.34 $^{\circ}$, Sponge@GO支架的接触角为62.23 $^{\circ}\pm$ 1.50 $^{\circ}$, 差异有统计学意义($P=0.000$), 见图1F。该结果显示, GO的加入不仅改变了支架的内部结构, 还增加了支架的吸湿性能。



Note: A. Appearance of Sponge. B. SEM image of Sponge. C. Appearance of Sponge@GO. D. SEM image of Sponge@GO. E. Water absorption. F. Contact angle.

图1 Sponge及Sponge@GO的形貌及吸湿性能

Fig 1 Morphology and hygroscopic properties of Sponge and Sponge@GO

2.2 生物相容性

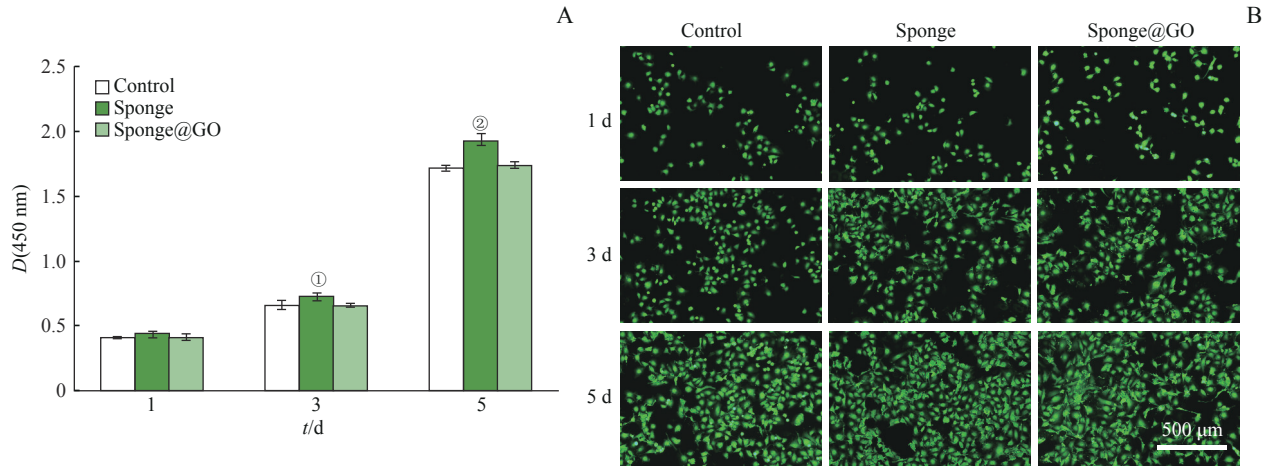
CCK-8法检测细胞毒性, 结果显示各组HUVECs随着时间推移, 吸光度均持续上升(图2A)。第3、5日, Sponge组细胞与对照组相比, 呈现出细胞增殖的状态(均 $P<0.05$); 而Sponge@GO组与对照组的

差异无统计学意义。细胞在第1、3、5日的活/死细胞染色结果(图2B)显示, Sponge组、Sponge@GO组和对照组均没有明显差异, 细胞分散较均匀, 呈现良好的增长态势。

通过SEM和荧光染色观察HUVECs在支架内部

的黏附能力。结果显示细胞在2种支架内部均可以沿纤维黏附并爬行生长, 形态伸展, 分布均匀, 而Sponge@GO内部的细胞数量明显较Sponge多(图

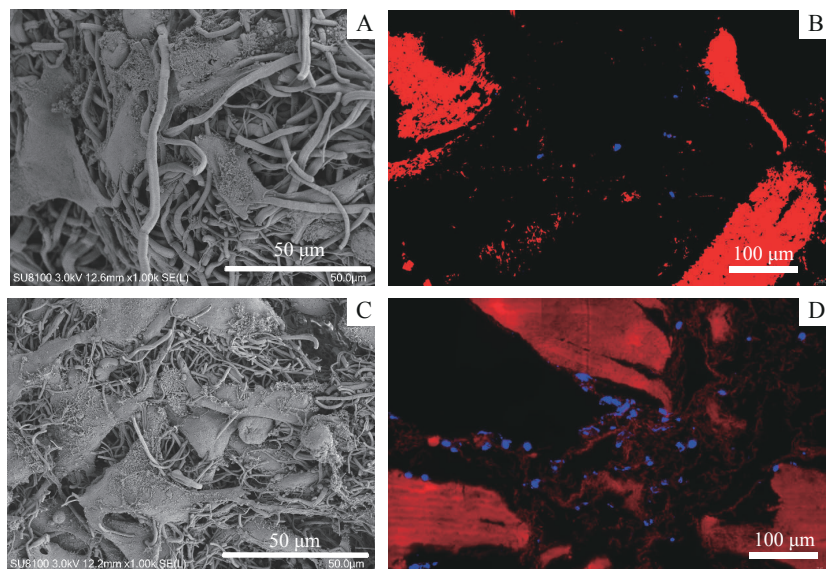
3)。该结果进一步证明了Sponge@GO的生物相容性良好, 并且具有更好的黏附能力。



Note: A. CCK-8. B. Live/dead staining. ^① $P=0.014$, ^② $P=0.000$, compared with the control group.

图2 Sponge及Sponge@GO的材料相容性

Fig 2 Biocompatibility of Sponge and Sponge@GO



Note: A. SEM images of HUVECs after 7 d of incubation on Sponge. B. Fluorescence staining of HUVECs after 7 d of incubation on Sponge. C. SEM images of HUVECs after 7 d of incubation on Sponge@GO. D. Fluorescence staining of HUVECs after 7 d of incubation on Sponge@GO.

图3 材料的细胞黏附性

Fig 3 Cell adhesion of the materials

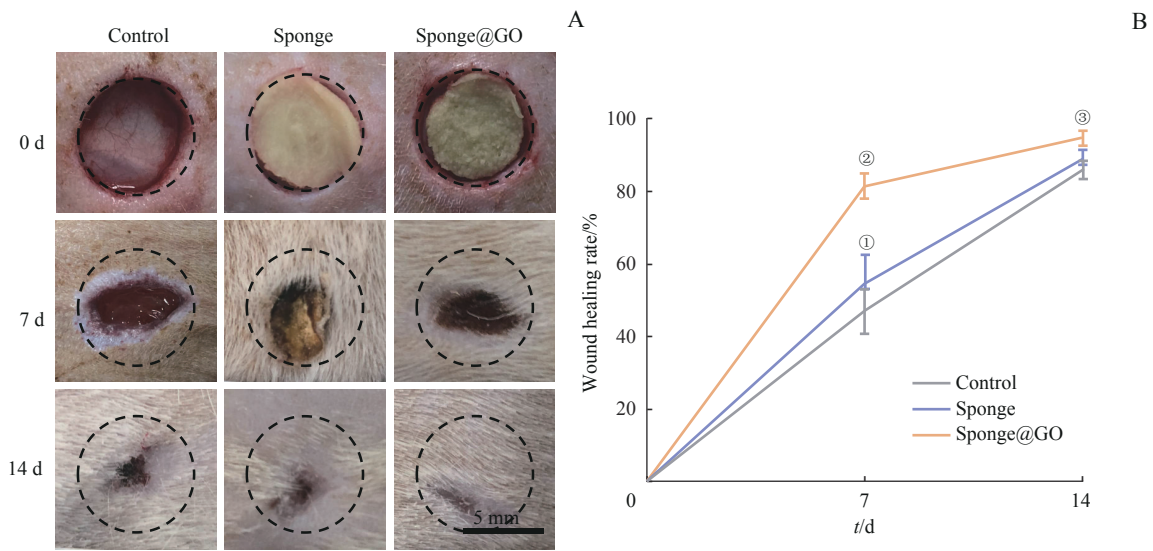
2.3 创面愈合情况

3组大鼠的创面均未见感染。随着时间推移创面逐步愈合, 且敷料逐渐降解, 并未对创面产生二次损伤(换药拍照使用生理盐水或碘伏润湿后进行)。第7日, 只有对照组创面可见少量出血, 而覆盖材料的大鼠创面干燥, 无明显渗出(图4A)。Sponge@GO组第7日的创面愈合率为(81.27±3.44)%, Sponge组为(54.41±7.94)%, 均显著高于对照组

[(46.85±6.15)%], 差异有统计学意义($P=0.000$, $P=0.024$); 第14日, Sponge@GO组的创面愈合率显著高于对照组($P=0.009$), 而Sponge组与对照组之间的差异无统计学意义(图4B)。

2.4 组织病理及免疫荧光染色观察

术后第7日, H-E染色结果显示对照组仍有较多的炎症细胞, 成纤维细胞较少; Sponge组开始出现较多



Note: A. Wound healing at Day 0, 7 and 14. B. Wound healing rate. ^① $P=0.024$, ^② $P=0.000$, ^③ $P=0.009$, compared with the control group at the same point.

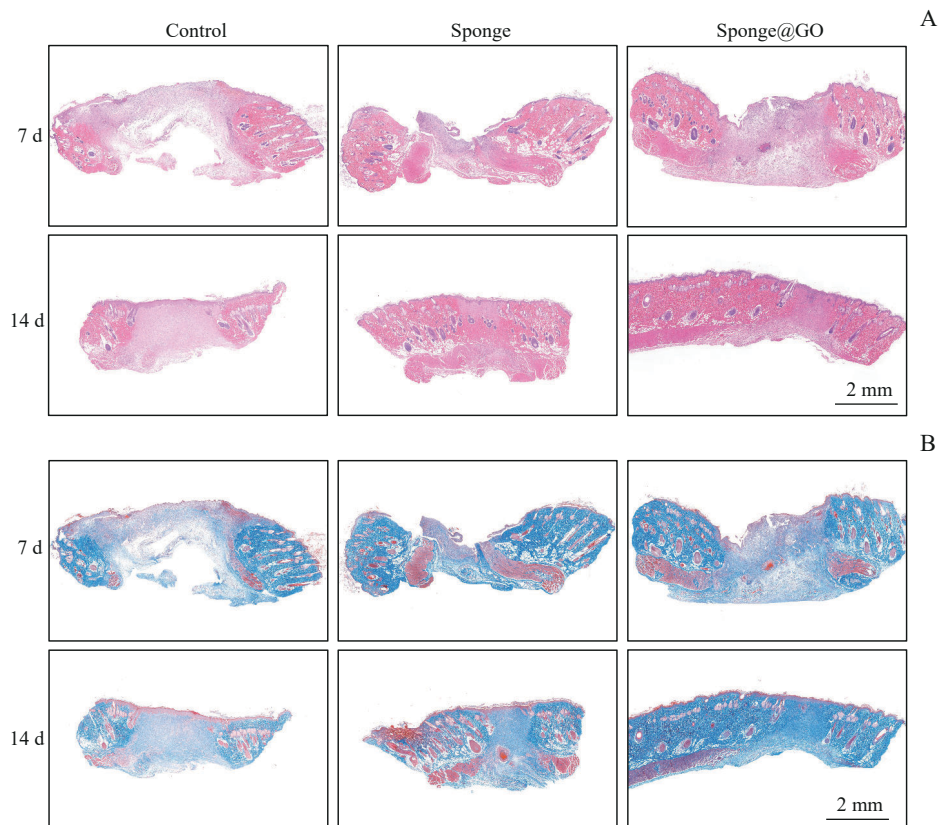
图4 糖尿病创面愈合情况观察($n=4$)

Fig 4 Observation of diabetic wound healing ($n=4$)

的成纤维细胞,但新生上皮爬行缓慢;Sponge@GO组可见表皮爬行,炎症细胞明显减少,创面明显缩小。第14日,3组创面均可见上皮不同程度的覆盖,Sponge组及Sponge@GO组开始出现皮肤附属器以及规则的真皮乳头层,尤其是Sponge@GO组的肉芽组

织更加成熟,结构更为均匀致密。详见图5A。

Masson染色结果(图5B)显示,蓝色胶原沉积量随创面的愈合而增加,特别是经Sponge@GO处理的创面,胶原在第14日时更加致密,上皮化显著,而对照组的胶原沉积较少。



Note: A. H-E staining. B. Masson staining.

图5 创面组织病理学观察

Fig 5 Histopathological observation of wound

α -SMA 免疫荧光染色结果 (图6) 显示, 第14日, 3组创面均开始出现有绿色荧光的新生血管, 对照组荧

光信号较弱, Sponge组和Sponge@GO组的荧光信号明显, 但后者的新生血管数量更多, 密度更高。

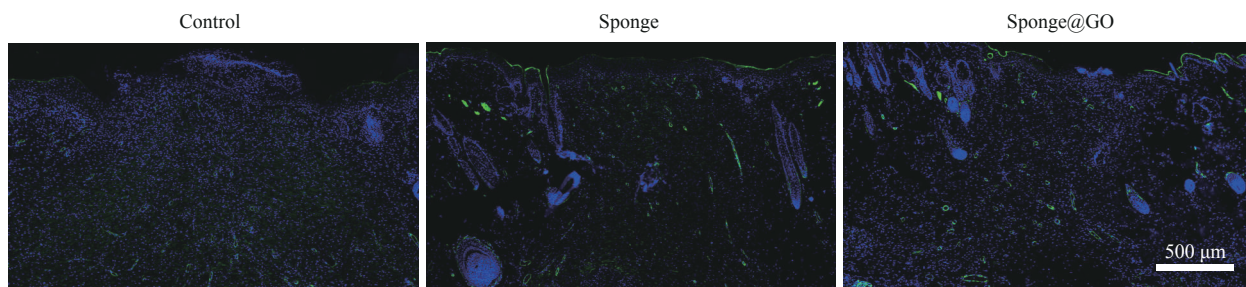


图6 术后第14日 α -SMA免疫荧光染色观察创面血管形成情况

Fig 6 Observation of angiogenesis by α -SMA immunofluorescence staining at Day 14

3 讨论

静电纺丝是电场作用下一种特殊的纤维制造工艺, 通过静电纺丝装置制备得到的纳米纤维材料一直是组织工程领域的研究热点^[23]。以往常用的二维结构电纺膜虽然具有类似细胞外基质的多孔结构, 但仍然无法真正模拟三维状态下的细胞生态位^[24]。将静电纺丝二维膜剪碎后, 再经均质化、塑形、交联等过程得到的三维立体结构短纤维支架, 解决了二维膜存在的一些限制, 例如机械性能较差、吸水率较低以及细胞无法纵向长入等^[16-17, 25-26]。本研究选用了常见的天然高分子材料明胶以及人工合成材料PLA, 不仅可以保证材料良好的生物相容性, 还可以提高相应的力学强度^[27-28]。明胶/PLA短纤维海绵支架制作简便, 并且比表面积及孔隙率均较高, 体外能够促进细胞的黏附增殖, 但仍缺乏特定的生物活性功能 (例如促血管生成等), 限制了其潜在应用。GO作为具有蛋白质吸附性能的生物活性纳米颗粒, 具备大量含氧基团, 不仅使材料的吸水性增强, 还可以进一步改变材料的内部结构, 增强材料的生物活性, 促进血管生成^[20, 29]。基于此, 本研究制备了一种负载GO的明胶/PLA短纤维海绵支架Sponge@GO, 该复合短纤维支架材料能够在体内达到良好的促创面愈合效果。而仅由短纤维堆积而成的三维网络结构缺乏纤维间的黏合性能, 缺乏稳定性, 因此需要通过交联来稳固其三维结构。常见的交联方式有热交联及化学交联, GO在热交联下会还原为石墨烯。因此, 本研究的短纤维海绵选用戊二醛进行化学交联, 并用谷氨酸溶液浸泡以减轻支架毒性^[22]。

经过SEM观察Sponge与Sponge@GO的内部结

构, 发现GO的加入并没有改变短纤维支架的多孔结构, 甚至孔隙率明显增大, 纤维直径明显减小。这是由于GO赋予了聚合物溶液更好的导电性能, 可以产生更细长的纳米纤维^[30], 孔隙率的增大也与纤维变细明显相关。除了孔隙率, 良好的吸水性能也为细胞生长、增殖、黏附以及后期创面愈合过程中的营养运输提供了重要条件。材料不仅可以吸收组织渗出液, 避免伤口浸渍, 同时又尽可能地为伤口提供微湿环境, 有利于创面修复。本研究制备的Sponge@GO, 吸水率约为Sponge吸水率的1.4倍, 接触角也显著缩小。这均与GO携带的亲水基团明显相关, 同时也验证了GO成功掺杂于纺丝纤维中。可见, Sponge@GO的高吸湿性能以及三维结构非常适合作为伤口敷料, 用于慢性创面。

材料的生物相容性对于体内实验的进一步开展至关重要。用材料的浸提液培养细胞后进行CCK-8法和活/死细胞染色观察, 发现Sponge@GO并未对细胞的生长、增殖产生抑制性影响。同时, 细胞在材料内培养7d后可沿纤维孔隙方向三维生长, 不断渗入支架内部, 特别是Sponge@GO内的细胞比Sponge内的细胞长入数量更多, 考虑与其高孔隙率及强吸水性有直接关系, 可以为细胞的黏附、浸润提供更好的生存环境。

DFU是糖尿病患者常见的并发症之一。虽然目前可通过自体皮肤移植、组织工程皮肤移植及各种敷料对糖尿病慢性创面进行治疗, 但仍无法从本质上解决血糖升高导致的血管生成障碍问题, 从而无法获得令人满意的治疗效果^[31]。因此, 无论是再上皮化, 还是新血管形成, 均是创面愈合的关键。本研究结果显示, GO的应用使糖尿病大鼠背部全层皮肤缺损创面在术后第7日表现出显著的缩小趋势, 第14日基本

趋于愈合,再上皮化以及胶原蛋白沉积方面均优于对照组以及Sponge组,组织结构完整、致密。胶原蛋白含量的升高及稳定还可以促进肉芽组织形成,进而加速伤口愈合。 α -SMA存在于血管平滑肌细胞中,可作为血管化的相关指标^[32]。有效的血管化为参与愈合的细胞提供充足的营养成分。本研究在术后第14日观察 α -SMA的免疫荧光染色情况,发现Sponge@GO组荧光信号更强,新生血管更多,密度更高。这表明负载GO的短纤维海绵在体内可以显著促进创面的愈合。

本研究构建了高亲水性静电纺丝短纤维海绵,并将其应用于动物糖尿病创面进行观察。体外实验结果表明,该材料具备良好的生物相容性及促细胞三维黏附生长性能,用于糖尿病全层皮肤缺损后可明显促进上皮化及胶原沉积,有利于创面愈合,缩短愈合时间。高亲水性静电纺丝短纤维海绵在促进血管生成及糖尿病慢性难愈性创面的治疗中可能具有重要的应用价值和临床意义。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

All authors disclose no relevant conflict of interests.

伦理批准和动物权利声明/Ethics Approval and Animal Right

本研究涉及的所有动物实验均已通过上海交通大学实验动物研究伦理委员会的审核批准(审批号SYXK 018-0027)。所有实验过程均遵照中国有关动物保护的指导方针和法律进行。

All experimental animal protocols in this study were reviewed and approved by the Experimental Animal Research Ethics Committee of Shanghai Jiao Tong University (Approval Letter No. SYXK 018-0027), and all experimental animal protocols were carried out by following China's guidelines and laws for animal protection.

作者贡献/Authors' Contributions

付晓晗、王娟参与了实验设计、论文写作,付晓晗负责数据分析,崔文国、王彦参与了技术路线指导及论文的修改。所有作者均阅读并同意了最终稿件的提交。

The study was designed by FU Xiaohan and WANG Juan. The manuscript was drafted by FU Xiaohan and WANG Juan. Data was analyzed by FU Xiaohan. CUI Wenguo and WANG Yan participated in technical route guidance and revision of the manuscript. All the authors have read the last version of paper and consented for submission.

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学术快讯

上海交通大学基础医学院方超课题组报道基于巨噬细胞的肿瘤靶向递药新技术

2023年2月12日,上海交通大学基础医学院方超教授团队在国际权威期刊 *Adv Funct Mater* 在线发表了题为 *Metal-coordinated adsorption of nanoparticles to macrophages for targeted cancer therapy* 的封面论文。该研究创建了一种简易、高效的胞外黏附纳米粒的巨噬细胞递药系统,为基于活细胞的高效递药系统的研发提供了新的平台技术。