中国激光

荧光碳量子点在生物医学研究中的前沿进展

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摘要 荧光碳量子点作为一种特殊的量子点，具有卓越的荧光性能以及可调控的表面化学性质，在生物成像、疾病诊断和治疗等生物医药领域中备受瞩目。基于近期的文献报道，详细介绍和总结了碳点在医药领域中的应用及其相关机制和特性。概述了碳点在生物医药应用中所面临的挑战，并提出了潜在的解决方案。最后，对未来的研究方向提出了建议，以期进一步拓展碳点在生物医药领域中的应用范围，为医学领域的创新和发展提供理论依据。

关键词 生物光学；碳量子点；生物成像；疾病诊断；疾病治疗

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1 引 言

碳点是一种尺寸在 10 nm 以内的荧光纳米材料。其制备方法多样而简便，原料来源广泛，光学性质稳定，具备强大的抗光漂白特性。与无机量子点相比，碳点不含重金属，因此具有较低的生物毒性和较高的生物相容性，在生物医学领域中具有广泛的应用潜力[1]。碳点表面具有丰富的官能团，这些官能团决定了其物理、化学和荧光性质，包括量子产率、发射波长、聚集诱导发射/猝灭、荧光寿命、生物相容性和特殊物质响应等[2]。其中，最重要的性质之一是其发光性质，其发光机制涵盖了多种机制，包括表面控制发光、交联增强发射效应、量子尺寸效应和碳核控制发光等[3]。这些机制相互作用，对其荧光效应产生影响。合理调控其发光性质，如荧光波长和荧光强度，对于疾病诊断具有重要意义。同时，通过对碳点表面官能团的调控，还可以调整其对活性氧（ROS）自由基等的清除能力。因此，碳点在疾病的治疗和诊断方面具有巨大的潜在发展潜力。碳点作为一种新型、低毒且光学性质优越的纳米材料，研究其在生物医药中的应用具有重要意义，可以为医学领域的创新和发展提供有力支持[4]。

自 2004 年研究者首次报道碳点以来，该领域引起了广泛的研究兴趣[5]。2007 年，Cao 等[6]发表了生物医学领域首篇涉及碳点的研究报告，即通过表面钝化的方法成功实现了纳米碳点的明亮光致发光。此外，碳点还展现出双光子发光特性，其双光子吸收截面与已有的高性能半导体量子点相媲美，成功地用于乳腺癌细胞的双光子发光显微镜成像。至今，碳点在生物医学领域中的应用已得到广泛报道，主要涵盖了生物成像[7]、疾病诊断[8]和疾病治疗[9]三个方面（图 1）。在本综述中，我们从生物医学应用最新进展及其作用机理两个方面，系统地介绍了近年来碳点在生物医学领域中的研究进展。最后，我们总结了碳点在生物医学应用中所面临的挑战，并对未来发展进行了展望。期望本文能够激发研究者进一步深入合作，推动碳点在生物医学领域中的实际应用，充分挖掘其潜在应用价值。

2 生物成像

为了观察机体组织、器官和细胞的生理状态，或者实现生命活动和细胞代谢过程的精确可视化，目前已有商业化的荧光小分子染料，如 4′,6-二脒基-2-苯基吲哚（DAPI）、尼罗红（Nile Red）和油红 O（Oil Red O）等，可用于细胞或细胞器成像。然而，这些染料中的大多数价格昂贵，需要复杂的有机合成，光学性质方面具有较小的斯托克斯位移，容易受到自我吸收影响，并且细胞器特异性较低。此外，这些染料中的许多只能用于固定细胞染色[10]。

纳米结构的碳点可以通过注射或口服方式进入机体，经由胞吞胞吐进入细胞[11]。它们可以分散于细胞质中或特异性结合于某些细胞器，这样一来，借助共聚焦显微镜或荧光活体成像等仪器，我们可以清晰地观察到机体结构如微血管、脑组织等的生理活动。同时，碳点还具有卓越的荧光性能，制备简单，原料成本低，抗光漂白性强，生物安全性高。因此，它们在生物成像方面具有很好的应用潜力。例如，Khan

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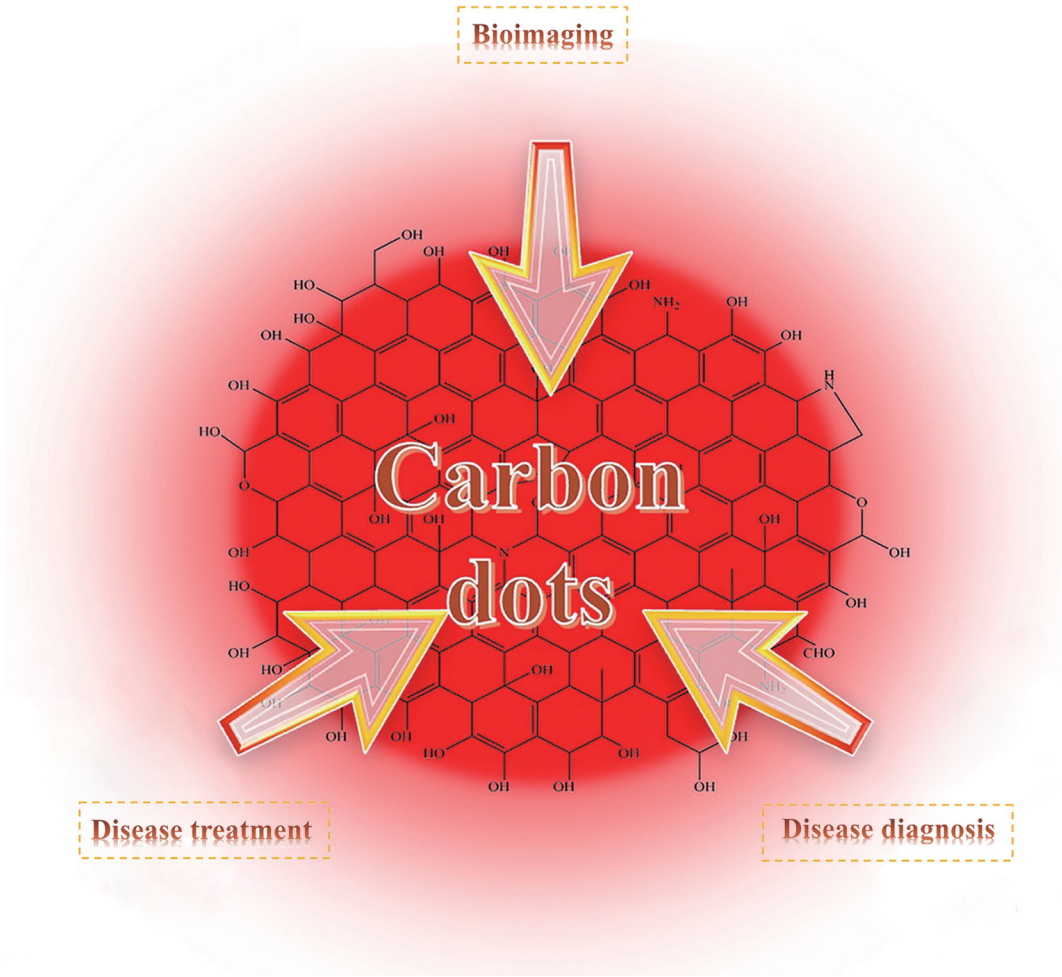


图 1　荧光碳量子点在生物医学领域中的应用研究

Fig. 1　Application research of fluorescent carbon quantum dots in biomedical field

等[12]成功设计了一种氮掺杂碳点，其具备良好的热稳定性，即使在 80 ℃下加热 1 h 后，碳点的性能依然非常稳定，而且在 20～80 ℃范围内都不发生热猝灭。此外，Nangan 等[13]通过简易的水热法，将废弃的聚四氟乙烯（PTFE）注射器制备成对哺乳动物细胞表现出轻微细胞毒性的碳点，使得在 1 mg/mL 质量浓度下细胞活力高达 91.07%。这一实验证明了碳点具有较高的生物相容性，并且表明碳点可以将持久性废弃物转化为有价值的多功能材料，减轻了环境压力。

近红外发光的碳点具备较强的组织穿透能力，对组织和肌肉的损伤较小，而且在成像方面表现出低自发荧光和高成像对比度。另外，长斯托克斯位移的碳点拥有更强的抗干扰性能。Domena 等[14]成功开发了一种长波长红色荧光的碳点，该碳点具有低毒性，并且对胶质母细胞瘤干细胞（GSC）表现出出色的红色荧光成像能力。在斑马鱼模型中，这些长波长红色荧光的碳点甚至能够穿越血脑屏障（BBB）。

2.1　细胞、细胞器成像

细胞和细胞器是人体正常生理活动的基本结构单元，监控其形态和状态对于维持生命活动具有重大意义。碳点可以通过监测细胞内环境的特征来进行细胞和细胞器成像，例如极性和电位等特性。由于溶酶体和线粒体富含脂溶性物质，故脂溶性药物更容易在这些细胞器内聚集成像[15]。此外，带有氨基基团的碳点更容易与带负电的细胞膜结合，从而实现细胞膜成像。通过靶向配体修饰，还可以实现对生物体特定部位的成像[16]。

溶酶体黏度是溶酶体微环境的重要参数，与多种疾病，包括癌症在内，密切相关。因此，准确量化溶酶体黏度的变化对于更好地理解溶酶体的动力学和生物学功能至关重要。研究者成功设计和开发了自靶向的橙红色荧光碳点，如图 2（a）所示，用于监测溶酶体黏度的波动。他们制备的橙红色荧光碳点可以迅速进入细胞进行溶酶体靶向成像，并实现活细胞和斑马鱼中黏度变化的可视化。这一研究成功追踪了溶酶体黏度在自噬过程中的变化，为可视化研究与溶酶体黏度相关的疾病提供了有力工具[17]。

细胞极性在许多病理和生理过程中扮演着至关重要的角色，例如，高尔基体的极性强烈影响细胞内蛋白质的加工和运输。然而，开发用于跟踪亚细胞极性变化水平的荧光探针仍然是一个巨大的挑战。在此背景下，研究者成功利用简单的溶剂热合成方法，通过混合

对苯二胺和乙二胺，设计并制备了一种具有出色高尔基体靶向能力和极性敏感特性的氨基封端碳点(CD)，如图 2(b)所示。这些碳点能够在细胞分裂和细胞凋亡过程中有效成像高尔基体的形态动力学变化，而叶酸修饰的 CD 则展现出与叶酸受体的高亲和力，可用于癌细胞的识别。值得注意的是，研究发现，凋亡细胞中的高尔基体的极性明显高于非凋亡细胞[18]。这一研究为实时跟踪高尔基体的变化和局部极性变化提供了可靠且稳定的方法，这表明 CD 在细胞凋亡评估和治疗药物筛选方面具有巨大的应用潜力。

2.2 组织活体成像

具有近红外荧光波长和高量子产量的荧光在活体成像中具有显著优势[10]。一旦进入体内，碳点通过血液循环最终在肾脏等部位排泄，这使得其在成像过程中具有一定的安全性[19]。脑胶质瘤是一种威胁生命的疾病。因此，早期诊断脑胶质瘤并在手术中进行准确定位对于改善预后至关重要。研究者利用微波法一步制备的环保绿色的锰掺杂的碳点作为磁共振(MRI)/光学双峰成像的纳米探针，如图 2(c)所示。这些超小尺寸的 Mn 掺杂碳点具有独特的激发依赖性光致发光发射特性、高弛豫性和低细胞毒性。小鼠脑胶质瘤的体内 MRI 和离体光学成像结果表明，掺杂 Mn 的碳点可能导致 MRI 纵向弛豫时间增加，微小神经胶质瘤的成像效果突出，这些 Mn 掺杂碳点作为 MRI/光学双模成像纳米探针，在微小脑神经胶质瘤的检测和手术定位方面具有巨大的应用潜力[20]。

荧光丝在纺织品、生物工程和医疗产品等领域中具有广泛的应用前景，然而，天然的家蚕丝几乎不具备荧光性。近期，研究者报道了一种由桑叶制成的碳点，如图 2(d)所示，这些 CD 表现出强烈的近红外荧光，绝对量子产率达 73%，并且其荧光禁带宽度为 20 nm。通过将这种 CD 加入蚕的饲料，研究人员观察到蚕产生了明亮的红色荧光，并且生长和成茧过程正常，最终蜕变成带有红色荧光的飞蛾。这些茧在日光下呈现粉红色，在紫外线下则发出鲜红色的荧光。经过孵化后，这些红色荧光飞蛾能够正常交配并产下发出荧光的卵。

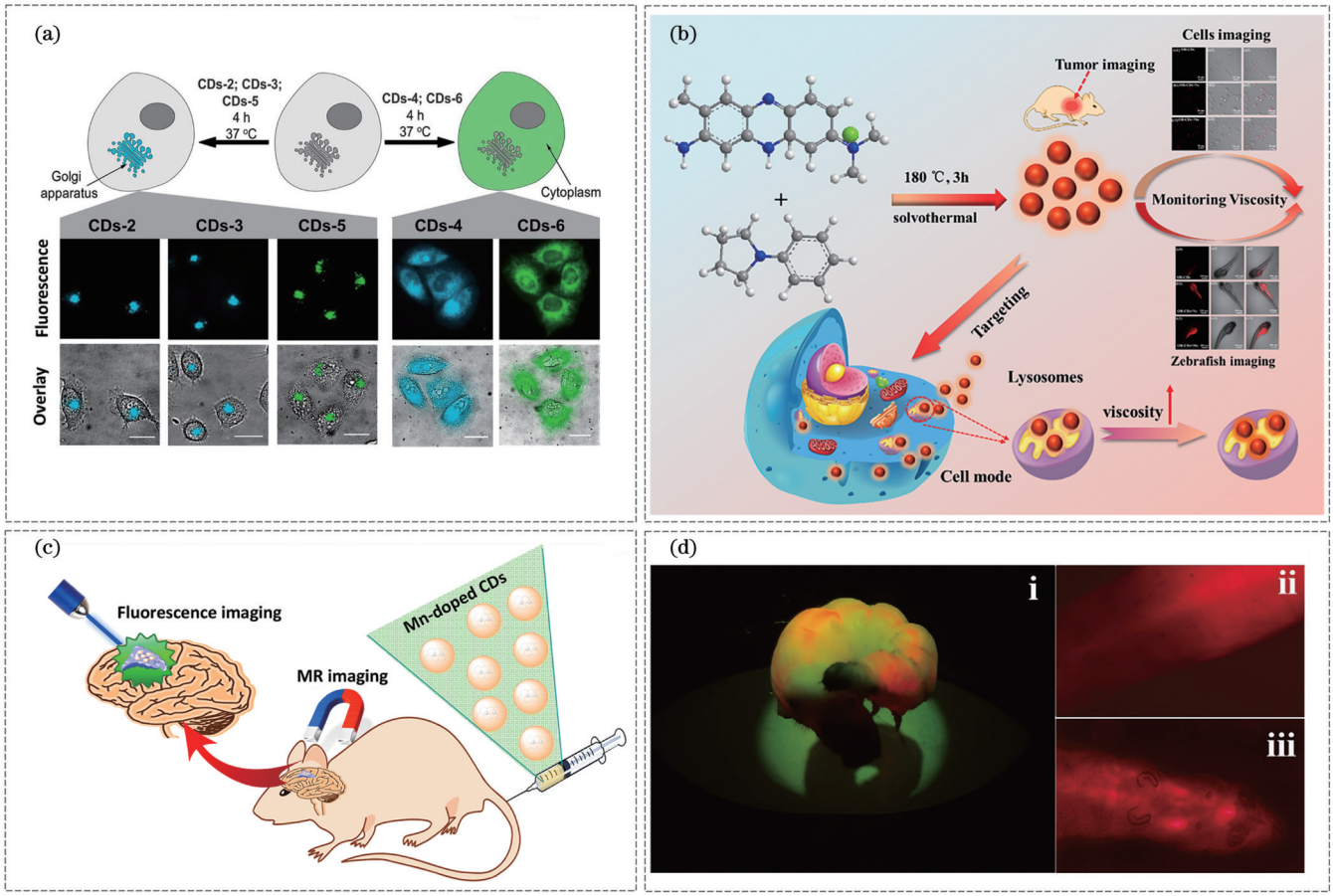


图 2 碳点在生物成像领域的应用。(a)六种碳点对 A549 细胞不同部位靶向成像的共聚焦荧光图像[17]；(b)碳点合成路线图及其在斑马鱼中的活细胞成像和活体成像[18]；(c)碳点用于小脑神经胶质瘤荧光成像和核磁成像的双模式成像示意图[20]；(d)碳点用于蚕的活体成像示意图[21]

Fig. 2 Application of carbon dots in field of bioimaging. (a) Confocal fluorescence images of six carbon dots targeting different parts of A549 cells[17]; (b) carbon point synthesis roadmap and its imaging *in vivo* and in living cells in zebrafish[18]; (c) dual-mode imaging diagram of carbon dots used for fluorescence imaging and nuclear magnetic imaging of cerebellar glioma[20]; (d) carbon point is used for *in vivo* imaging of silkworm[21]

进一步的实验发现，第二代蚕的生长周期与对照组相似，这表明这种CD具有出色的生物相容性。通过对测试蚕和茧进行解剖和分析，可揭示CD的代谢途径：蚕会通过消化道吸收荧光CD，然后将其转移到丝腺，最终转移到茧中，而未被吸收的CD则会随着粪便排出[21]。在这整个碳点消化过程中，蚕都具有良好的生命状态，并且在蚕的生长繁殖过程中碳点的荧光都未发生猝灭现象，都能观察到鲜红的荧光。这些结果都证实了该CD具有优异的生物相容性和荧光稳定性。

3 疾病诊断

碳点在生物医药领域中的另一个重要应用是疾病的诊断。与其他创伤性诊断方法相比，碳点用于诊断时具有更低的创伤性[22]，因此在疾病诊断方面具有广阔的应用前景[23]。

3.1 生理环境诊断

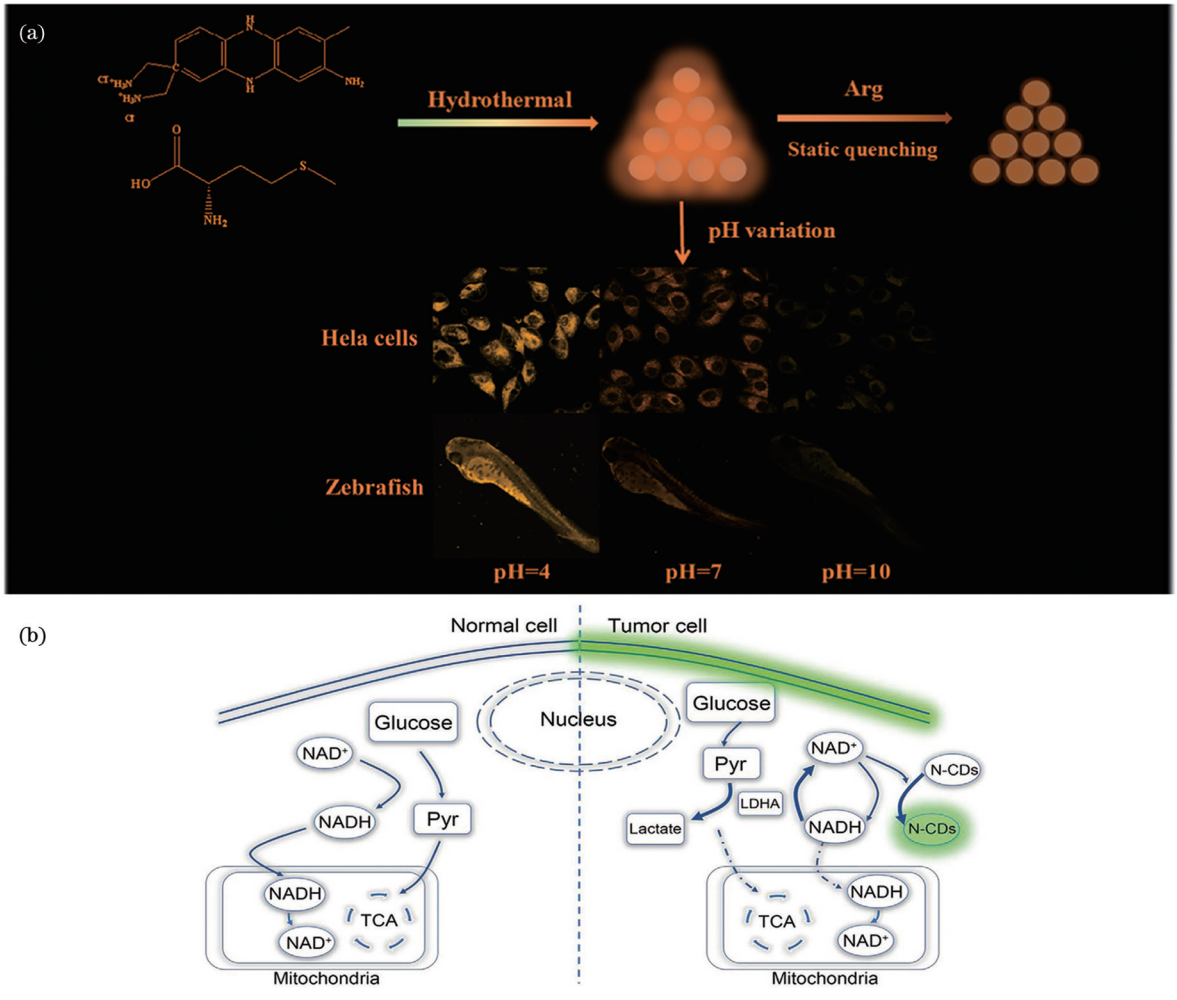
生理环境在疾病的发生和发展中起着至关重要的作用，涵盖了黏性、极性和酸碱性等多个方面。通过对生理环境的诊断，我们能够判断疾病的发生和发展，从而实现提前预测和治疗的目标[24]。细胞内的pH值与细胞周期以及多种生理和病理过程密切相关，例如细胞凋亡、受体介导的信号传导、离子转运、肌肉收缩、炎症和肿瘤生长。因此，准确测定pH值对于早期疾病诊断至关重要。研究者设计了一种N和S共掺杂的碳点，如图3(a)所示，其具有长波长的发射，表现出独特的pH敏感发光特性，碳点的荧光强度与pH值在pH值为4.8～8.0时呈现出良好的线性关系，是生理环境中用于pH监测的潜在成像试剂。此外，由于其出色的生物相容性和低细胞毒性，这些碳点可用于体内和体外的pH和精氨酸(Arg)成像[25]。

研究者报道了一种烟酰胺腺嘌呤二核苷酸氧化诱导的氮掺杂碳点发出的荧光增强策略，如图3(b)所示，用于监测肿瘤的发生并提供肿瘤形成的早期预警。该策略设计制备的碳点表现出出色的区分肿瘤细胞和正常细胞的能力，因此可用于评估肿瘤细胞的增殖。这一策略已在49个临床样本中得到了验证，其在患者样本中的灵敏度达到了79.31%，同时在健康受试者样本中未观察到荧光信号[26]。

3.2 生物标志物响应

除了监测疾病的生理环境外，碳点还能对某些生物标志物产生选择性响应，从而导致荧光信号的变化，如荧光强度[11]、波长[27]、寿命[28]、峰形[29]等。

例如，恶性肿瘤由于其高发病率和致死率而成为全球人类健康的重大威胁之一。对肿瘤的发生和发展



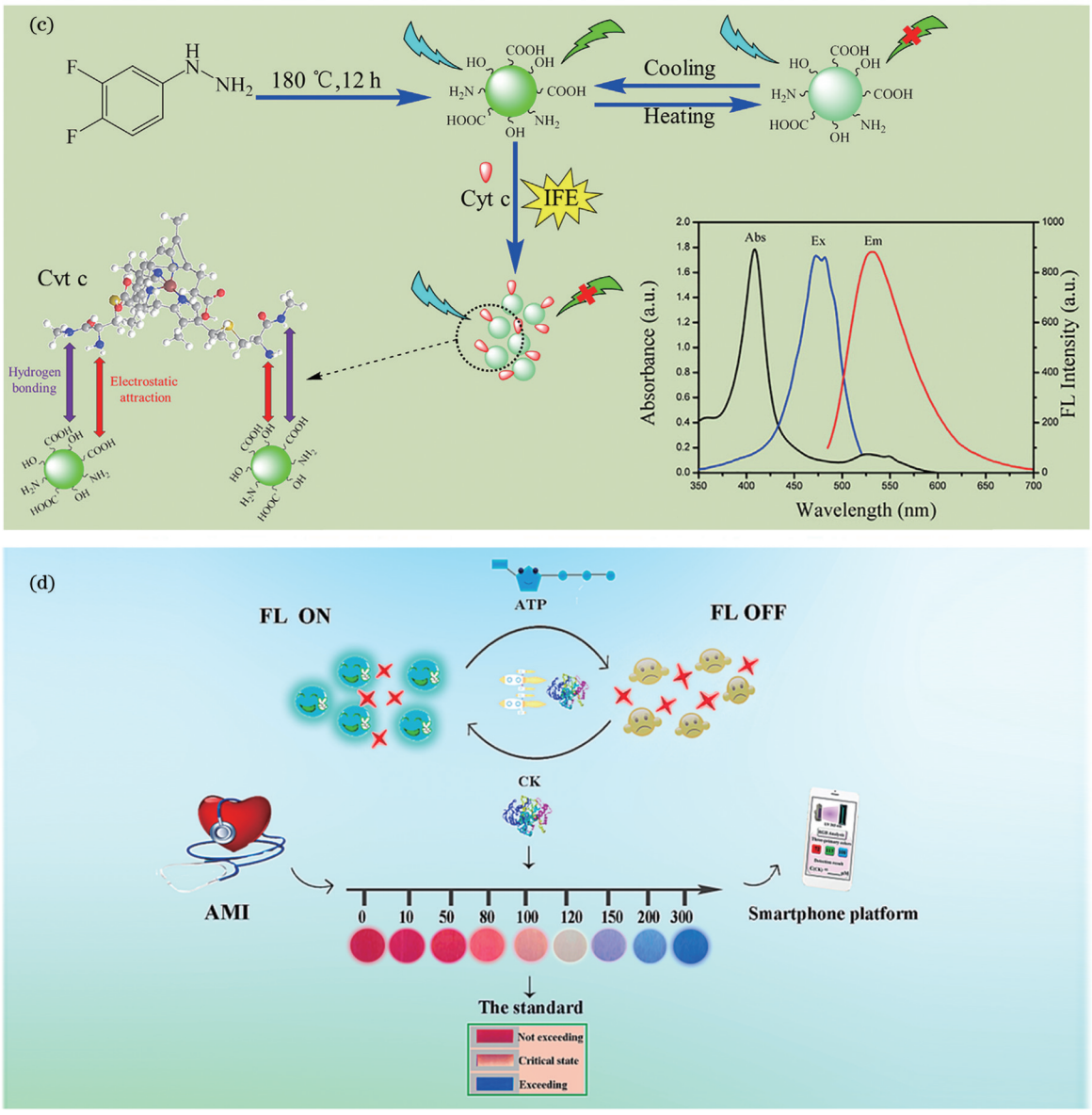


图 3 碳点在疾病诊断领域的应用。(a)碳点监测斑马鱼和活细胞内环境 pH 变化的示意图[25];(b)碳点传感体内糖酵解机制图[26];(c)碳点的制备及细胞色素 C 的传感机理[31];(d)将制备的比例荧光碳点用于 ATP 和肌酸激酶(CK)的荧光传感和视觉检测[32]

Fig. 3 Application of carbon point in field of disease diagnosis. (a) Carbon point monitoring of environmental pH changes in zebrafish and living cells[25]; (b) map of glycolysis mechanism of carbon point sensing *in vivo*[26]; (c) preparation of carbon points and sensing mechanism of cytochrome C[31]; (d) prepared proportional fluorescent carbon points are used for fluorescence sensing and visual detection of ATP and creatine kinase (CK)[32]

进行监测对于更好地理解肿瘤的病理过程至关重要。在多种肿瘤类型中,能量代谢模式从氧化磷酸酶化转变为有氧糖酵解,因此可能出现与肿瘤的发生和发展密切相关的特殊代谢模式[30]。

作为重要的生物标志物,细胞色素 C(CytC)的分析对于细胞凋亡和癌症诊断至关重要。Zhu 等[31]开发了一种无标记的探针,如图 3(c)所示,这些碳点的平均直径为 3.4 nm,能够形成相当稳定的具有黄绿色荧光的胶体溶液。其具有相对较高的荧光量子产率,达到 16.9%。该方法已成功用于人类血清样品中 CytC 的检测,回收率在 93.14%~110.40% 之间。

肌酸激酶(CK)作为心脏损伤的重要生化指标,对于急性心肌梗死或心脏骤停的早期准确诊断具有重要意义。然而,CK 检测的敏感性和特异性研究仍然存在挑战。研究者设计并制备了一种比率荧光碳点,如图 3(d)所示,该探针在腺嘌呤核苷三磷酸(ATP)存在时对 CK 表现出超快的荧光响应,CK 浓度与荧光回收率之间呈现出良好的线性关系,检测限低至 1.20 U/L(U/L 为每升液体含有的酶活力单位)。机理研究表明,“ON-OFF-ON”过程可归因于比率荧光碳点与 ATP 相互作用形成的非发光基态复合物(比率荧光碳点-ATP),在 CK 的催化下复合物会发生解离,从而产生荧光恢复现象。此外,由于其优秀的生物相容性,比率荧光碳点可进一步应用于活细胞成像。值得注意的

是,通过结合比率荧光探针和智能手机颜色识别应用,已经开发了便携式视觉传感平台[32]。

4 疾病治疗

碳点具有丰富的表面状态[33],能与机体发生多种化学反应,在疾病治疗中具有广泛的应用。此外,选择药物作为碳点的前体在制备过程中,除了具有卓越的荧光性能外,还能保留部分药物活性基团[34-35],从而实现诊断与治疗的一体化[36]。碳点在疾病治疗中的应用主要包括以下三个方面:肿瘤治疗[37]、抗菌与抗病毒治疗[38]及抗炎症治疗[39]。

4.1 肿瘤治疗

近年来,纳米材料在癌症治疗中崭露头角,与传统癌症治疗方法相比,纳米治疗具有微创性和对正常组织毒性较小的优点。碳点是生物医学领域中具有前景的纳米材料,具有出色的生物相容性、独特的物理化学性质和易于表面修饰的特性,可形成多功能纳米平台,有效用于抗肿瘤治疗[40]。

碳点作为荧光探针、药物载体、肿瘤诊断试剂等,在肿瘤治疗领域中得到广泛应用。碳点具有丰富的官能团和大的π共轭体系,因此易于修饰并与其他材料结合,形成多功能纳米平台。一方面,碳点可以作为药物分子和功能蛋白的载体,共同实现治疗功能。另一方面,碳点可以与其他纳米材料结合,形成多功能复合材料。这不仅可以提高材料在治疗过程中的稳定性,还可以赋予材料对多种刺激的响应能力,显示出协同治疗的优势。碳点在肿瘤治疗方面的应用方式包括光动力疗法、光热疗法、声动力学治疗、化学动力学治疗、饥饿疗法和基因治疗(GT)等[41]

Deng等[42]通过水热法使用二甲双胍和没食子酸前体合成了一种新型的碳点,如图4(a)所示,这种新型的碳点可以用于胶质母细胞瘤的治疗。这些碳点具有穿越血脑屏障的能力,表现出敏感的抗肿瘤活性,具有出色的靶向肿瘤细胞线粒体的能力,并且无需额外的靶向分子的辅助,这导致了线粒体收缩和线粒体嵴数量的减少。转录组分析表明,碳点通过抑制磷脂磷酸酶4(PLPP4)的表达来干扰甘油磷脂的代谢途径,从而诱导铁死亡。在人源原位胶质母细胞瘤小鼠模型中,这项工作进一步证实了碳点的有效治疗效果。Han等[43]使用菲咯啉介导的配体辅助策略制备了具有高吡咯氮含量和超小尺寸的碳点支撑的Fe单原子纳米酶,如图4(b)所示。这些碳点通过协同化学动力学和光热效应,在体外和体内有效抑制了肿瘤细胞的生长。与此同时,研究者制备了功能化的核靶向橙光发射负载阿霉素的碳点(CDs-NLS-DOX),从而获得了核靶向的橙光发射药物递送系统。与游离的阿霉素(DOX)相比,CDs-NLS-DOX表现出更强的抑制肿瘤生长的能力。CDs-NLS-DOX有望成为一种用于肿瘤治疗的高精度和高效的核靶向纳米药物递送系统。

4.2 抗菌与抗病毒治疗

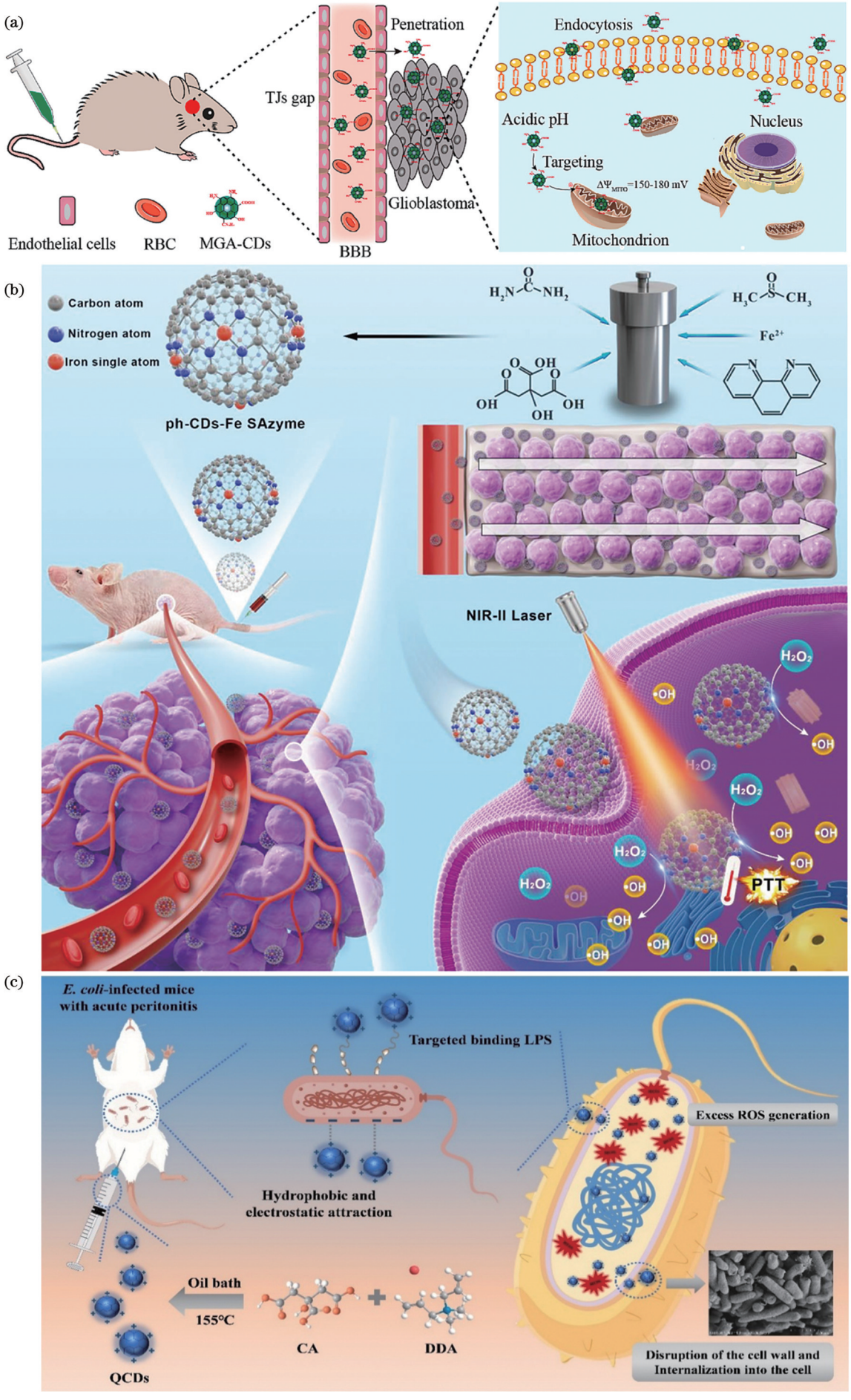
细菌感染和炎症问题对人类健康和社会经济构成了严重威胁。随着超级细菌的出现和抗生素耐药性问题的恶化,寻找新型抗菌药物变得至关重要。功能化碳点,由于其低细胞毒性、高生物相容性以及与传统抗生素不同的抗菌机制,被认为可能成为治疗细菌感染性疾病的新平台。这些碳点具有出色的膜通透性,能够抑制细菌的外排泵机制,并通过产生活性氧或自由基来抑制细菌脂质的过氧化,从而发挥抗菌作用。重要的是,它们的抗菌机制与传统抗生素不同,因此不容易导致细菌耐药性。碳点的抗菌机制主要包括共价和非共价相互作用、活性氧产生、光热疗法等[44]。

碳点可以与细菌发生共价和非共价相互作用,如静电相互作用、化学键相互作用和疏水相互作用,从而有效地缩短碳点与细菌之间的距离,导致细菌的聚集。这会造成细菌细胞壁的损伤,导致细菌细胞内物质,如脱氧核糖核酸(DNA)、核糖核酸(RNA)、ATP和核糖体等的泄漏,从而产生强烈的抗菌作用。研究人员合成的季铵化碳点(QCDs)具有带正电的性质,如图4(c)所示,表现出有效的广谱抗菌活性,并增强了对革兰氏阴性菌的抑制能力。此外,QCDs在不同细胞中表现出低毒性,并且不会引起溶血。与硫酸庆大霉素治疗的阳性对照组相似,QCDs表现出了消除感染和炎症的治疗效果,因此被认为是一种有望成为革兰氏阴性细菌感染新疗法的候选材料[45]。

活性氧具有强烈的氧化能力,碳点所产生的ROS能够扩散至细菌细胞内,破坏细菌的结构和成分,干扰细菌的生理活动,从而达到有效的杀菌效果,因此碳点成为抗菌材料的有力候选者。研究者采用一锅式水热法成功合成了增强抗菌活性且耐药性低的左氧氟沙星碳点(LCD),如图4(d)所示。研究结果表明,LCD既保留了左氧氟沙星的活性基团,具有出色的抗菌性能,同时又能够通过其表面正电荷产生活性氧的特性来破坏细菌。此外,体外和体内实验进一步证实了LCDs在抗菌和生物相容性方面的卓越表现,为其在抗菌医学领域中的潜在应用提供了支持。碳点也展现出卓越的抗病毒能力。研究者成功合成了天然碳点(NCQD),并通过抗病毒研究揭示,表面钝化的NCQD在应对Covid-19危机方面具有显著潜力,对SARS-CoV假病毒细胞的抑制率高达85%。

4.3 抗炎治疗

活性氧和炎症是伤口愈合受阻的关键因素。过量的ROS会引发炎症,抑制血管生成和肉芽组织形成,延迟进入增殖期,最终导致受损组织的再生和皮肤伤口的愈合延迟。因此,去除体内过度生成的ROS和消除炎症是促进伤口修复的关键[46]。近年来,研究者们发现碳点在抗炎和抗氧化方面具有巨大潜力。碳点作为抗炎剂的机制与其结构密切相关。首先,碳点通过清除ROS、下调促炎细胞因子的表达,以及与细胞受体结合来调节


(a)
Penetration
TJs gap
Glioblastoma
BBB
Endothelial cells
RBC
MGA-CDs
Endocytosis
Acidic pH
Nucleus
Targeting
ΔΨMITO=150-180 mV
Mitochondrion
(b)
Carbon atom
Nitrogen atom
Iron single atom
ph-CDs-Fe SAzyme
Fe2+
NIR-II Laser
H2O2
•OH
PTT
(c)
E. coli-infected mice with acute peritonitis
Targeted binding LPS
Hydrophobic and electrostatic attraction
Oil bath
155°C
CA
DDA
QCDs
Excess ROS generation
Disruption of the cell wall and Internalization into the cell

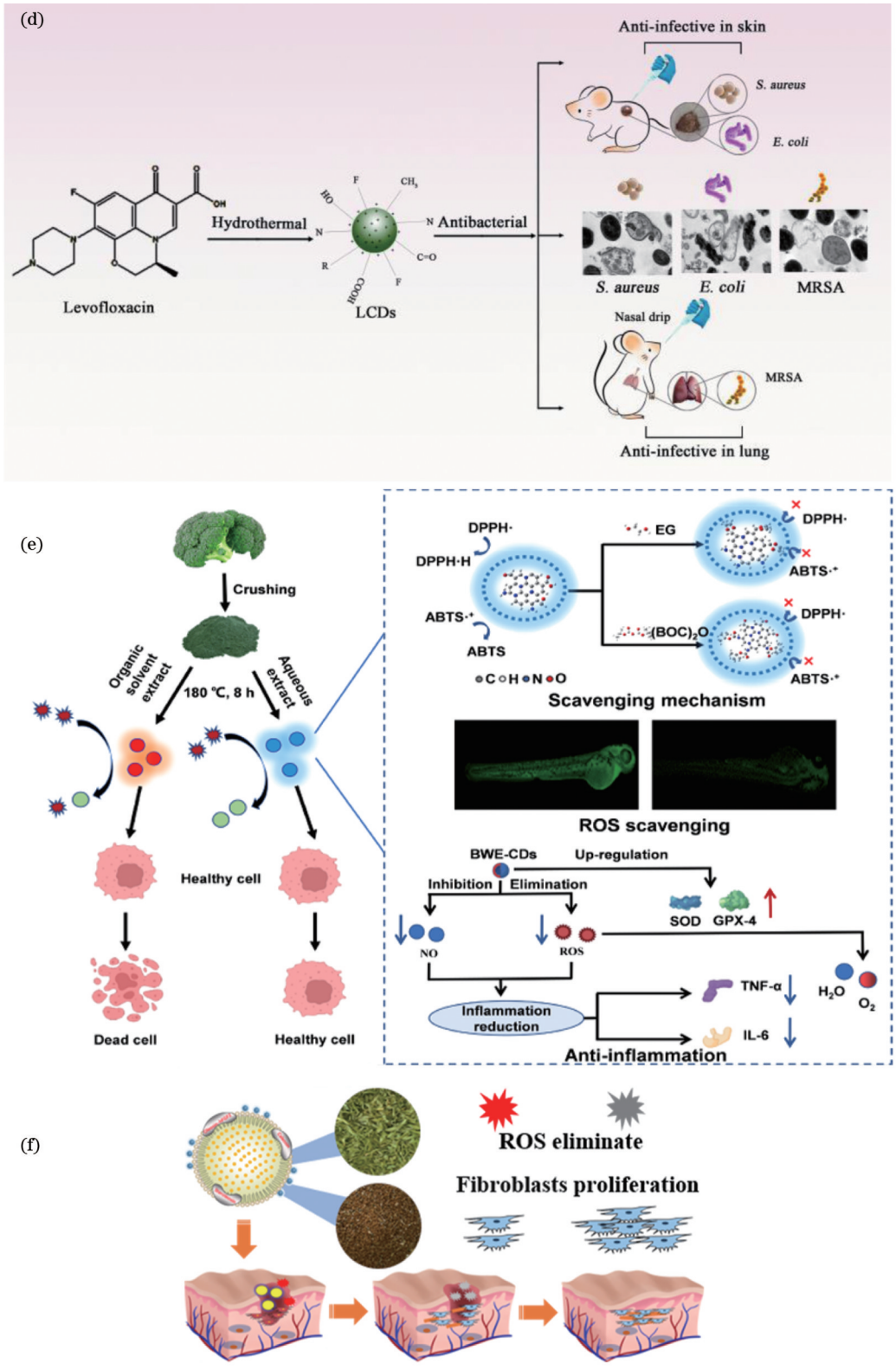


图 4 碳点在疾病治疗方向的应用。(a)碳点穿透血脑屏障并靶向线粒体治疗肿瘤的示意图[42];(b)碳点的制备流程及光疗化疗协同治疗小鼠肿瘤示意图[43];(c)季铵化碳点的合成及抗菌机制示意图[45];(d)左氧氟沙星碳点的制备及对小鼠抗菌治疗的示意图[50];(e)西兰花源碳点清除ROS治疗细胞和斑马鱼炎症的示意图[48];(f)亚麻荠碳点通过清除ROS和抗炎加速伤口修复示意图[49]

Fig. 4 Application of carbon point in direction of disease treatment. (a) Schematic of carbon dots penetrating blood-brain barrier and targeting mitochondria for tumor therapy[42]; (b) preparation process of carbon point and schematic of phototherapy and chemotherapy synergistic treatment of mouse tumor[43]; (c) synthesis of quaternary ammoniated carbon points and schematic of antibacterial mechanism[45]; (d) preparation of carbon points of levofloxacin and schematic of antibacterial therapy in mice[50]; (e) schematic of broccoli source carbon point clearing ROS for treatment of inflammation in cells and zebrafish[48]; (f) schematic of cardamine carbon points accelerate wound repair by removing ROS and anti-inflammatory [49]

细胞反应，具有显著的内在抗炎特性。某些疾病，如类风湿性关节炎、炎症性肠病(IBD)和过敏，因为慢性炎症或自身免疫反应而引起免疫系统的失调。碳点具有作为治疗剂的潜力，可以恢复免疫系统的平衡[47]。

碳点的表面具有许多氧化的化学活性基团，如酚羟基，容易与氧化物质发生反应，从而发挥抗氧化和抗炎作用。Deng等[48]通过优化前体、提取溶剂以及使用西兰花作为生物原料制备了碳点，如图4(e)所示。与西兰花水提物、西兰花粉和西兰花有机溶剂提取物相比，源自西兰花水提物的碳点(BWE-CDs)由于其表面含有丰富的C═C、羰基和氨基基团，具有出色的抗氧化性能和卓越的安全性。它有效地清除了A549细胞、293T细胞和斑马鱼体内的活性氧，并缓解了内毒素(LPS)刺激下斑马鱼的炎症。机理研究表明，BWE-CDs的抗炎作用取决于碳点与自由基的直接反应。

碳点可以作为纳米酶发挥抗炎和抗氧化的作用。Zhang等[49]合成了一种新型亚麻荠衍生碳点(CDs)，如图4(f)所示，并将其装饰在连接了人成纤维生长因子(hFGF2)的亚麻荠脂滴(CLD-hFGF2)上，形成了纳米生物材料CDs-CLD-hFGF2。CDs-CLD-hFGF2具有过氧化物酶活性，能够有效清除活性氧自由基，并在体外成功促进NIH/3T3细胞对氧化应激的应对。在急性伤口模型中，经CDs-CLD-hFGF2治疗后伤口愈合率在第10天达到了近92%，而CLD-hFGF2为82%。此外，伤口部位显示出明显的抗炎效果，表现为促炎因子的下调和抗炎因子水平的上调。因此，CDs-CLD-hFGF2被视为一种有效的皮肤伤口愈合方法。

在碳点上保存抗氧化活性基团有助于疾病治疗。研究者制备了一种具有荧光和双重抗炎作用的纳米药物递送系统。他们成功将甘草酸和甲氨蝶呤负载到碳点上，设计制备的纳米给药系统的可溶性微针显著抑制了促炎细胞因子的分泌，对关节炎具有显著的治疗效果。因此，所制备的甘草酸-碳点-甲氨蝶呤可溶性微针为治疗类风湿性关节炎提供了一种可行的方案。

5 瓶颈与展望

尽管性能各异的荧光碳点在生物医学领域中得到了广泛的应用，但在合成、性能调控和应用等方面仍存在一些挑战。首先，设计合成碳点需要综合考虑各种制备条件对其表面状态、尺寸和结构的影响，以实现对这些关键特性的精确控制，从而获得在生物医药领域具有高效性的碳点。调节各种制备条件以实现精确控制仍然是一个挑战。其次，虽然碳点在生物成像及疾病诊断和治疗等领域中具有潜在的应用价值，但将其应用转化为实际产品仍然面临挑战。需要进一步解决性能可靠性、成本效益、大规模制备等方面存在的问题，以推动碳点技术的商业化发展。最后，随着碳点应用的推广，相关法规和标准变得越来越重要。制定相关的标准、规范和指导方针是确保碳点应用程序的质量、安全性和可靠性的有效措施。尽管存在这些挑战，但科学家们仍在努力解决上述难题，推动碳点制备技术的发展和应用。

在过去的几年里，研究人员广泛研究了碳基新型发光纳米材料。在本综述中，我们旨在综合近年来的研究进展，总结碳点在生物医药领域中的应用，包括生物成像及疾病诊断和治疗，如表1所示。此外，我们也系统概述了碳点领域所面临的挑战。

尽管碳点领域存在众多困难和挑战，但其卓越的光学性能和多样的物理化学性质使其在生物医学领域中具有不可替代的优势，包括安全性、可持续性、易获得性和性能可调性。期待未来研究能够更快推动碳点应用于实际生活，实现商品化、产业化和工业化应用。

表1 近几年碳点在生物医药领域中的应用总结

Table 1 Summary of application of carbon points in biomedical field in recent years

Object	Application	Property	Detail	Year	Ref.
CDs	Bioimaging	Polarity-sensitive and Golgi targeting	Golgi imaging and real-time tracking	2023	[17]
OR-CDs		Viscosity sensitive and lysosomal targeting	Lysosome imaging and viscosity change monitoring	2023	[18]
Mn-doped CDs		Green synthesis and low cytotoxicity	Imaging of brain glioma by fluorescence and MRI	2018	[20]
CDs		Biocompatibility, high quantum yield, and fluorescence stability	Imaging of silkworm and producing fluorescent silk	2022	[21]
N, S-CDs	Disease diagnosis	pH and arginine sensitivity, biocompatibility, and low cytotoxicity	Physiological environment pH detection	2023	[25]
N-CDs		Being specific for glycolytic metabolism	Cellular glycolysis imaging	2021	[26]
N, F-CDs		Cytochrome C sensitivity, temperature sensitivity, and high quantum yield	Recovery of CytC from serum	2021	[31]
BN-L-CDs		Dual wavelength emission, low toxicity, and sensitivity and specificity to creatine kinase	Visual detection of heart disease	2023	[32]

续表

Object	Application	Property	Detail	Year	Ref.
MGA-CDs	Disease treatment	Blood-brain barrier permeability and tumor mitochondrial targeting	Intracranial tumor suppression	2023	[42]
pH-CDs-Fe		Peroxidase activity, photothermal effect, and chemodynamic therapeutic properties	Tumor cell therapy	2018	[43]
QCDs		Broad-spectrum antibacterial activity and inhibition of Gram-negative bacteria	Polar peritonitis caused by escherichia coli	2023	[45]
LCDs		Low drug resistance, antimicrobial activity, and biocompatibility	Bacterial infection and animal infection with pneumonia	2022	[50]
BWE-CDs		Green, low toxicity, and antioxidant and anti-inflammatory activity	Treating inflammation in zebrafish	2023	[48]
CDs-CLD-hFGF2		Peroxidase activity and free radical scavenging activity	Skin wound healing	2023	[49]

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Recent Advancements in Biomedical Research on Fluorescent Carbon Quantum Dots

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Abstract

Significance Research on quantum dots has attracted significant attention since the Nobel Prize in Chemistry was awarded to scientists in this field. As a special type of quantum dots, fluorescent carbon quantum dots (CDs) have excellent fluorescence and controllable surface chemical properties, which can be applied in biological medicine fields such as bioimaging and diagnosis and

treatment of diseases. CDs are fluorescent nanomaterials with a size of less than 10 nm. Their preparation methods are diverse and simple, precursors are widely available, optical properties are stable, and photobleaching resistance is strong. Compared with inorganic quantum dots, they do not contain heavy metals, so they have lower biotoxicity and higher biocompatibility, and have great application potential in the biomedical field. The surface of CDs is rich in functional groups, which determine their physical, chemical, and fluorescent properties, including quantum yield, emission wavelength, aggregation-induced emission/quenching, fluorescence lifetime, biocompatibility, and special material response. One of their most important properties is luminescence, which comprises a variety of mechanisms, including surface-controlled luminescence, cross-linked enhanced emission effect, quantum size effect, and carbon core-controlled luminescence. These mechanisms interact with each other to influence the CD fluorescence effect. Reasonable regulation of the CD luminescence properties, such as fluorescence wavelength and intensity, is of great significance in disease diagnosis. At the same time, through regulation of the surface functional groups of CDs, the scavenging ability of ROS free radicals can be adjusted. Therefore, CDs have great application potential in the diagnosis and treatment of tumors and inflammation.

Progress Based on recent literature reports, this study introduces and summarizes in detail the application of CDs in the field of biomedicine and their related mechanisms and characteristics. First, in terms of biological imaging, CD nanostructures enter cells through endocytosis and exocytosis and disperse in the cytoplasm or specifically in some organelles. As a result, we can clearly observe the physiological activities of body structures such as micro vessels and brain tissue with the help of confocal microscopy or other instruments [Figs. 2(a) and (b)]. The design and preparation of CDs with near-infrared fluorescence wavelength and high quantum yield result in higher resolution and tissue penetration ability, which is advantageous for *in vivo* imaging [Figs. 2(c) and (d)]. On this basis, we introduce the application of CDs in disease diagnosis. Compared with other diagnosis methods, the application of CDs is less traumatic, which opens up broad prospects in disease diagnosis. CDs with pH-sensitive luminescence characteristics can be used as potential imaging reagents for pH monitoring [Fig. 3(a)]. Fluorescence enhancement strategies based on nitrogen-doped CDs induced by nicotinamide adenine dinucleotide can be used to monitor tumor occurrence and provide early warning of tumor formation [Fig. 3(b)]. CDs can also produce selective responses to some biomarkers, resulting in changes in fluorescence signals, which can play a role in monitoring the occurrence and development of diseases through the detection of cytochrome C in human serum samples [Fig. 3(c)] and creatine kinase (CK), an important biochemical indicator of heart injury [Fig. 3(d)]. Finally, CDs with rich surface states can interact with the body in a variety of chemical reactions. CDs designed and prepared with specific structures can be effective in disease treatment, mainly in the following three areas: 1) tumor treatment, 2) antibacterial and antiviral treatment, and 3) anti-inflammatory treatment. A novel CD for the treatment of glioblastoma was synthesized using metformin and gallic acid precursors [Fig. 4(a)], whereas Fe single-atom nano cases with high pyrrole nitrogen content and ultra-small CD support were prepared using a phenazoline mediated ligand-assist strategy [Fig. 4(b)]. CDs effectively inhibit the growth of tumor cells through synergistic chemical kinetics and photothermal effects. The synthesized quaternary ammonium CDs have positive charge properties and can retain antibiotic precursor active groups [Figs. 4(c) and (d)], leading to effective antimicrobial activity. The surface of CDs has many oxidized chemically active groups, such as phenolic hydroxyl, which react easily with oxidizing substances, thus playing antioxidant and anti-inflammatory roles. Anti-inflammatory and antioxidant CDs are prepared through precursor optimization, solvent extraction, and use of broccoli as a biological feedstock [Fig. 4(e)]. CDs can also be designed as nano-enzymes to perform anti-inflammatory and antioxidant functions [Fig. 4(f)]. At the end of the paper, we outline the challenges faced by CDs in biomedical applications. First, for efficient application of CDs in biomedical fields, various preparation conditions need to be considered comprehensively to achieve accurate control of their key properties. Second, the conversion of CDs into actual products still faces challenges, and further solutions are needed to promote their production and commercialization. Finally, the regulation and standardization of CDs are becoming increasingly important. To solve the above problems, the development and application of CD preparation technology should be promoted.

Conclusions and Prospects CDs are being widely used in the field of biomedicine, including bioimaging and diagnosis and treatment of diseases (Table 1). Their excellent optical, physical, and chemical properties provide them with obvious advantages in the field of biomedicine, including safety, light stability, easy access, and performance tunability. In the future, the large-scale and diversified development of CDs can be further enhanced to promote their industrial production, commercialization, and application in real life.

Key words bio-optics; carbon quantum dots; bioimaging; disease diagnosis; disease treatment