GLUT1靶向型中药活性成分纳米递送系统的研究进展

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［摘要］ 肿瘤细胞在缺氧条件下利用糖酵解为其提供物质与能量，满足快速生长和增殖的能量需求，即“Warburg效应”。即使在有氧条件下，肿瘤细胞也主要依靠糖酵解提供能量。因此，参与葡萄糖代谢过程中的葡萄糖转运蛋白1（GLUT1）在肿瘤发生、发展及耐药中发挥着重要作用，被认为是恶性肿瘤治疗的重要靶点之一。近年来，肿瘤糖代谢方面的研究逐渐成为热点。已有研究表明，多种因子参与对肿瘤能量代谢的调控，其中尤以GLUT1的作用最为关键。该文综述了GLUT1靶向型中药活性成分纳米递送系统在肿瘤治疗中的最新研究进展，旨在揭示GLUT1靶向型中药活性成分纳米递送系统在化疗药物递送的可行性和有效性。GLUT1靶向型中药活性成分纳米递送系统可以克服传统靶向策略及高渗透长滞留（EPR）效应的瓶颈。综上所述，GLUT1靶向型中药活性成分纳米递送系统为肿瘤的靶向治疗提供了新的策略，并在肿瘤的预防和治疗中具有广阔的应用前景。

［关键词］ 葡萄糖转运蛋白1（GLUT1）；靶向；药物递送系统；Warburg效应；肿瘤微环境；高渗透长滞留效应；中医药
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GLUT1-targeted Nano-delivery System for Active Ingredients of Traditional Chinese Medicine：A Review

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［**Abstract**］ Tumor cells use glycolysis to provide material and energy under hypoxic conditions to meet the energy requirements for rapid growth and proliferation，namely the Warburg effect. Even under aerobic conditions，tumor cells mainly rely on glycolysis to provide energy. Therefore，glucose transporter protein 1

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(GLUT1), which is involved in the process of glucose metabolism, plays an important role in tumorigenesis, development and drug resistance, and is considered to be one of the important targets in the treatment of malignant tumors. In recent years, research on tumor glucose metabolism has gradually become a hot spot. It has been shown that various factors are involved in the regulation of tumor energy metabolism, among which the role of GLUT1 is the most critical. In this paper, the authors reviewed the latest research progress of GLUT1-targeted traditional Chinese medicine (TCM) active ingredient nano-delivery system in tumor therapy, aiming to reveal the feasibility and effectiveness of this system in the delivery of chemotherapeutic drugs. The GLUT1-targeted TCM active ingredient nano-delivery system can overcome the bottleneck of the traditional targeting strategy as well as the high-permeability long retention (EPR) effect. In summary, the authors believe that the GLUT1-targeted TCM active ingredient nano-delivery system provides a new strategy for targeted treatment of tumors and has a broad application prospect in tumor prevention and treatment.

[**Keywords**] glucose transporter protein 1 (GLUT1); targeting; drug delivery system; Warburg effect; tumor microenvironment; high-permeability long retention effect; traditional Chinese medicine

癌症是目前人们所面临的一个重要健康问题，同时也是导致人们死亡的主要原因之一，严重影响人们的生活质量[1]。化疗是癌症的主要治疗方式之一，但结果往往不令人满意，并伴有一定不良反应[2]。传统的化疗药物包括紫杉醇、顺铂和阿霉素等缺乏对肿瘤的靶向性，临床应用时容易导致药源性肾损伤等不良反应[3-5]。特别是高剂量的化疗药物用于肿瘤治疗容易使肿瘤细胞产生耐药性，治疗效果有限[6]。因此，如何提高抗肿瘤药物的靶向性是目前药物递送系统研究的关键性问题。

随着生物化学理论的不断完善，研究人员逐渐发现肿瘤细胞的生长和增殖依赖于能量的不断供给，而葡萄糖则是肿瘤细胞能量的主要来源[7]。有氧糖酵解是肿瘤“糖代谢异常”的标志之一，葡萄糖通过有氧糖酵解在这种“糖代谢异常”肿瘤细胞中进行代谢重编程。实体瘤的一个普遍特点是即使在氧气含量正常的情况下，葡萄糖摄取量和乳酸的积累量也会逐渐升高[8]。目前的研究显示，葡萄糖进入细胞的过程中需要葡萄糖转运蛋白的参与，而在众多的葡萄糖转运蛋白中又以葡萄糖转运蛋白1(GLUT1)的作用最重要[9]。具体而言，肿瘤细胞通过GLUT1将葡萄糖通过细胞膜转运到肿瘤细胞中，在肿瘤细胞中通过一系列糖酵解酶的作用产生丙酮酸，丙酮酸产生乙酰辅酶A进入三羧酸循环，为肿瘤细胞的生长和增殖提供能量。此外，GLUT1表达上调可以提高有氧糖酵解的效率，以促进葡萄糖有效进入肿瘤细胞并参与代谢[10]。与正常细胞相比，肿瘤细胞更容易出现“葡萄糖饥饿”，主要表现为肿瘤细胞中葡萄糖摄取率增加和糖代谢产物的乳酸含量升高[11]。进一步研究表明，GLUT1在肺癌[12]、肝癌[13]、黑色素瘤[14]、乳腺癌[15]、卵巢癌[16]、结直肠癌[17]等多种肿瘤中的表达均升高，使得肿瘤细胞能够大量摄入葡萄糖来满足肿瘤细胞的能量需求。

目前，随着对肿瘤能量代谢关系的深入研究，基于肿瘤细胞内存在的糖代谢异常，GLUT1介导的药物递送逐渐引起研究人员的关注[18]。一方面GLUT1可以调控肿瘤能量代谢，通过靶向GLUT1直接阻断肿瘤细胞的能量来源，从而实现将肿瘤细胞“饿死”[19]。另一方面，GLUT1介导的药物递送系统可以将药物主动转运至肿瘤细胞，诱导肿瘤细胞凋亡[20]。GLUT1参与肿瘤细胞中葡萄糖的基础水平吸收。抑制GLUT1可减少肿瘤细胞增殖并诱导肿瘤细胞损伤。天然GLUT1抑制剂的研究程度较低，已知的天然GLUT1抑制剂的结构仅限于几种天然产物，如人参皂苷Rh_2[21]、红景天苷[22]、小檗碱[23]、葛根素[24]、人参皂苷Rg_3[25]等。因此，发现和研究其他天然GLUT1抑制剂用于肿瘤的靶向治疗至关重要。在该篇综述中，总结了基于GLUT1介导的中药活性成分递送策略及其在癌症治疗中的最新进展，希望基于GLUT1靶向的中药活性成分递送策略在癌症治疗中发挥巨大潜力。

1 Warburg效应介导的肿瘤异常糖代谢

肿瘤细胞利用糖酵解作为主要能量代谢的来源，获得更高的葡萄糖分解能力，使得葡萄糖转变为乳酸来产生三磷酸腺苷(ATP)，这种现象称为“Warburg效应”。Warburg效应代表着肿瘤细胞对葡萄糖利用方式由氧化磷酸化到糖酵解的转变[26]。这种能量代谢的改变受复杂因素的调控，包括肿瘤微环境的压力和基因的改变等[27]。特别的是“Warburg效应”在增强糖酵解作用的同时抑制线粒

体氧化磷酸化[28]。

Warburg效应诱导肿瘤细胞出现异常糖代谢，因此肿瘤细胞需要通过GLUT1摄取大量的葡萄糖满足其能量需求[29]。因此，GLUT1可作为葡萄糖转运的一个限速因素，在肿瘤的能量代谢中发挥了至关重要的作用[30]。值得注意的是，肿瘤细胞的快速增殖使得肿瘤内部处于缺氧状态，与有氧呼吸相比，无氧条件下糖酵解生成的ATP量极少，因此肿瘤细胞需要大量表达GLUT1来满足其对能量的需求，这使得GLUT1已成为潜在的肿瘤治疗靶点之一[31]。目前的研究显示，肿瘤细胞中GLUT1的表达增多能够加速细胞对葡萄糖的摄取，为糖酵解提供充足的原料，促进ATP的生成，而糖酵解过程中的中间产物可以合成脂肪酸、核酸，并调节细胞代谢及生物合成，从而促进肿瘤的生长、转移及耐药等过程[32-34]。

糖酵解过程中与肿瘤相关的关键代谢酶包括GLUT、己糖激酶（HK）、6-磷酸果糖激酶（PFK）亚型和丙酮酸激酶（PK）[35-37]。在这个过程中，葡萄糖通过细胞膜表面的GLUT1进入肿瘤细胞，进入细胞的葡萄糖通过HK转化为不能穿过细胞膜的葡萄糖-6-磷酸，从而将葡萄糖限制在细胞内[38]。最近的研究表明电刺激肿瘤细胞后，细胞膜破损导致GLUT1表达下调，可以抑制肿瘤细胞能量代谢[39]。一些类黄酮可以通过抑制GLUT1来增加癌细胞对化疗药物的敏感性[40-42]。此外，葡萄糖诱导的蛋白激酶B/哺乳动物雷帕霉素靶蛋白（Akt/mTOR）激活在急性髓系白血病中起着促进生长的作用，抑制糖酵解将是急性髓系白血病的重要辅助治疗策略[43]。研究显示，和厚朴酚可通过抑制缺氧诱导因子表达进而下调GLUT1表达，从而阻止乳腺癌生长[44]。

肿瘤细胞增殖过程需要大量的ATP，因此需要增加对葡萄糖的吸收，以及提高有氧糖酵解的效率，有氧糖酵解将葡萄糖转化为丙酮酸，最终导致乳酸产量增加[45-46]。值得注意的是，肿瘤细胞内的乳酸外流可调节肿瘤微环境，包括细胞侵袭[47]、血管生成[48]、肿瘤耐药[49]、转移发展[50]和逃避免疫监视[51]，来促进肿瘤进一步发展。GLUT1主要负责葡萄糖摄取，特别是在肿瘤细胞的有氧糖酵解过程中，与肿瘤的进展密切相关[52-53]。目前的研究表明，GLUT1在肿瘤细胞中的高表达是肿瘤治疗的潜在靶标，肿瘤细胞GLUT1受体的高表达可以促进Warburg效应[54]。例如，根皮素可以结合恶性肿瘤细胞上高表达的GLUT1并被细胞摄取[55]。因此，研究人员构建一个具有GLUT1肿瘤靶向能力的自组装谷胱甘肽响应系统，可以用于有效的基因递送和癌症治疗[56]。传统中药紫草的活性成分是一种萘醌化合物紫草素，研究表明紫草素和顺铂联合用药可下调肿瘤组织中丙酮酸激酶2（PKM2）及其转录调控的下游基因GLUT1的表达[57]。β-乳香酸（β-BA）是民间药物齿叶乳香的主要成分，据报道对包括肿瘤在内的各种疾病有效。研究显示，β-BA可以通过GLUT1靶向诱导的糖酵解抑制和腺苷酸活化蛋白激酶（AMPK）/mTOR通路的改变来缓解体内和体外癌前病变[58]。

2 GLUT1靶向型中药活性成分纳米递送系统

药物递送系统为肿瘤的精确定位和早期诊断、靶向、长效和联合治疗提供了重要的研发平台，为克服传统药物非特异性靶向和非选择性损伤正常组织的瓶颈问题提供了可能[59-61]。GLUT1靶向型中药活性成分纳米递送系统因其生物安全性和肿瘤靶向性而在肿瘤治疗方面引起了相当大的关注[62]。鉴于肿瘤细胞通过Warburg效应上调GLUT1的表达，研究人员利用GLUT1介导的肿瘤细胞转吞作用开发了一系列GLUT1靶向型中药活性成分纳米递送系统。GLUT1靶向型中药活性成分纳米递送系统大致可分为无机纳米颗粒、两亲性胶束、无载体前药、多糖-金属复合物、多酚纳米颗粒及脂质体。本文系统总结了各种GLUT1靶向型中药活性成分纳米递送系统在肿瘤治疗中的应用。

2.1 无机纳米颗粒 无机纳米颗粒具有良好的可降解性在肿瘤诊断和治疗领域具有相当大的应用潜力[63]。最近的研究显示，无机纳米颗粒在化疗药物递送方面取得一系列进展[64-66]。然而，由于缺乏足够的靶向能力，无机纳米颗粒作为药物递送系统时容易脱靶以至于化疗药物在肿瘤内的蓄积不足，严重影响化疗药物的治疗效果[67-68]。因此，随着精准医学的发展和对肿瘤糖代谢异常机制的进一步深入研究，GLUT1靶向修饰无机纳米颗粒用于肿瘤诊断和治疗逐渐引起研究人员关注。

纳米羟基磷灰石（HAP）具有良好的生物相容性和生物活性，且对肿瘤细胞具有选择性抑制作用[69]，因此，其有望成为新型的无毒、无不良反应的纳米药物递送系统，但其疏水性和肿瘤靶向性差严重阻碍了其在肿瘤治疗领域中的应用[70]。为了解决这些问题，CHENG等[71]制备了一种由聚丙烯酸（PAA）、HAP和吲哚菁绿（ICG）组成的有机-无机杂化纳米体系，并用葡萄糖进一步修饰，得到靶向纳米药物（GA@HAP/ICG-NPs）。体外细胞实验证实，

GA@HAP/ICG-NPs通过GLUT1介导的内吞作用显着促进细胞摄取并增加细胞内ICG和Ca^{2+}浓度。过量的Ca^{2+}诱导的线粒体损伤协同光动力治疗/光热治疗进一步诱导肿瘤细胞凋亡。原位近红外(NIR)进一步显示,肿瘤组织有更多的药物蓄积,这与细胞摄取实验结果相一致。综上,GA@HAP/ICG-NPs具有良好的GLUT1肿瘤靶向能力和抗肿瘤效果,有望进一步用于临床试验。

2.2 胶束 近年来,聚合物胶束因其具有稳定性好、可增加药物溶解度、载药能力强、不良反应少和提高药物的生物利用度等优点被广泛研究[72-73]。目前,已有负载化疗药物的聚合物胶束制剂上市使用,并且在临床前及临床试验中得到深入研究,证明了聚合物胶束在递送化疗药物中的巨大潜力[74]。然而,传统的聚合物胶束缺乏足够的肿瘤靶向性导致肿瘤部位药物蓄积不足。

随着精准医学的发展,GLUT1靶向修饰的聚合物胶束逐渐引起研究人员关注。LI等[75]提出了一种新的"瓣膜关闭"饥饿策略,通过关闭转运到肿瘤细胞中的葡萄糖的"瓣膜"来放大化疗效果,该策略由GLUT1抑制剂染料木黄酮(Gen)和化疗剂姜黄素(Cur)共负载的杂化有机硅胶束纳米药物来实现,具有可控的稳定性。体内外实验结果表明,纳米药物可以通过抑制GLUT1表达(即"瓣膜关闭")诱导肿瘤细胞饥饿,有效降低肿瘤细胞中葡萄糖/ATP的水平,从而削弱肿瘤细胞对化疗引起的细胞凋亡的抵抗力,有助于提高抗肿瘤效率,并基于GLUT1抑制诱导的应激敏化作用将不良反应降至最低。目前的研究表明,线粒体是癌症治疗中引人注目的靶标[76]。因此,WEI等[77]构建了一种GLUT1靶向型聚酰胺/雷公藤红素(PAMAM/Cel)胶束,用于缺氧激活的线粒体特异性药物递送和光热疗法,以抑制肿瘤生长和转移。在化疗和光热疗法的协同下,PAMAM/Cel胶束通过GLUT1靶向肿瘤并在荷瘤裸鼠的线粒体中积累,从而对肿瘤生长和转移具有优异的抑制作用。

2.3 无载体前药 无载体纳米前药可经EPR效应聚集于肿瘤部位释放活性化疗药物,同时兼具超高载药量和控释等优点,作为新兴的药物递送系统受到研究人员的广泛关注[78]。然而,与其他纳米药物一样,无载体纳米前药在肿瘤部位和肿瘤细胞中的蓄积不足是限制其临床转化的一大难题[79]。此外,实体瘤的异质性也导致无载体前药难以有效实现无载体纳米前药的精准递送和均匀释放药物[80]。

目前的研究显示,基于GLUT1靶向的前药因其水溶性和靶向性优异逐渐引起研究人员关注[81]。RAMÍREZ等[82]设计并合成了雷公藤内酯醇(TG)-葡萄糖偶联物的6种位置异构体(TG1α、TG1β、TG2、TG3、TG4和TG6)。这些偶联物表现出更好的水溶性,在高表达GLUT1的肿瘤细胞和低表达GLUT1的非肿瘤细胞之间具有选择性细胞增殖抑制性。最后,WANG等[83]基于Warburg效应的靶向策略设计了一系列新型秋水仙碱糖缀合物作为微管蛋白聚合抑制剂,然后评估秋水仙碱糖缀合物对三种人类癌症系HT-29、MCF-7和Hep-3B的抗增殖活性。其中,秋水仙碱糖缀合物在GLUT1高表达细胞(HT-29和MCF-7)和GLUT1低表达细胞(Hep-3B)之间的选择性>10倍,并且对HUVECs的细胞增殖抑制活性也低于秋水仙碱。此外,秋水仙碱糖缀合物显著抑制微管蛋白聚合并破坏微管网络。GLUT1抑制剂依赖性细胞毒性试验表明,秋水仙碱糖缀合物的摄取通过GLUT1进行调节。总之,GLUT1靶向型无载体前药可以通过GLUT1介导的靶向递送,随后释放药物实现肿瘤的精准治疗。

2.4 多糖纳米颗粒 多糖是一类潜在的生物材料,由于其优异的生物相容性和可修饰性逐渐被用于纳米递送系统的设计和开发,尤其是对于肿瘤免疫联合治疗具有重要意义[84]。多糖基纳米药物通过响应肿瘤内部[pH[85]、活性氧(ROS)[86]、ATP[87]、谷胱甘肽GSH[88]、酶[89]、缺氧环境[90]]或外部刺激(温度[91]、光[92]],能够实现在肿瘤部位的有效积累,并实现药物的控制释放,最终提高治疗效果。值得注意的是,部分多糖如透明质酸[93]和岩藻多糖[94]还可作为靶头赋予纳米系统主动靶向能力,而壳聚糖[95]、肝素[96]、葡聚糖[97]能够增强药物的治疗作用。

顺铂是常用的一线化疗药物,但溶解度低[98]、靶向性差[99]、容易耐药[100]和不良反应大[101]等问题限制其临床应用。为了解决当前顺铂在肿瘤治疗中的局限性,SHARMA等[102]通过加氏乳杆菌中提取的胞外多糖和顺铂配位制备了加氏乳杆菌多糖-顺铂复合物。加氏乳杆菌多糖-顺铂复合物上的葡萄糖残基可以靶向肿瘤细胞表面的GLUT1受体,进而增强顺铂的靶向性。此外,与顺铂相比,加氏乳杆菌多糖-顺铂复合物可以提高顺铂的水溶性和半衰期,且具有极高的安全性。值得注意的是,中药天然多糖-铂配位复合物可以成为一种有效且更安全的策略,在增强或保留顺铂活性的同时最大限度减少毒副作用和不良反应[103-106]。此外,岩藻多糖是

含岩藻糖的复杂硫酸化多糖，具有显著的抗癌作用，但由于岩藻多糖的复杂性，结构与抗癌活性关系很难确定。目前的研究表明岩藻多糖及其衍生物有效抑制了MDA-MB-231细胞的线粒体膜电位，降低了GLUT1的表达。MDA-MB-231细胞与岩藻多糖衍生物和寡霉素（氧化磷酸化抑制剂）的共同处理产生了协同抗癌作用[107]。

2.5 多酚纳米颗粒 天然多酚化合物可以诱导肿瘤细胞凋亡，并具有调节肿瘤相关信号通路和免疫检查点的功能[108-109]。此外，具有抗氧化能力的多酚基纳米药物可以打破肿瘤微环境的氧化还原平衡，从而辅助一系列基于氧化应激的治疗，如光热疗法[110]、化学动力学疗法[111]、放射动力学疗法[112]等。然而，传统的多酚基纳米药物在实体瘤内的蓄积不足限制了其临床应用[113]。

为了提高多酚基纳米药物在实体瘤内的蓄积能力，LI等[114]利用天然多酚类化合物聚多巴胺纳米颗粒（PDA NPs）、葡萄糖基功能配体以及硼替佐米（BTZ）开发了一种新型GLUT1靶向纳米药物。葡萄糖基功能化的PDA NPs可以通过肿瘤细胞表面的GLUT1受体有效地积累在肿瘤部位，并定位在肿瘤细胞的亚细胞内/溶酶体中，并且能够响应肿瘤微环境和内/溶酶体pH及光热疗法，以促进BTZ的释放。因此，这种GLUT1靶向、pH和光热响应性的纳米药物显示出肿瘤治疗临床转化的巨大潜力和临床转化前景。此外，研究显示超小粒径纳米颗粒更容易实现在实体瘤内的滞留和渗透，这与实体瘤的血管通透性有关[115-117]。因此，YUE等[118]基于Fe^{3+}和中药活性成分芦丁（RH）的生物矿化反应构建了GLUT1靶向超小纳米探针用于三阴性乳腺癌（TNBC）的精确诊断和治疗。在纳米探针中，黄酮醇中央支架以及葡萄糖苷和鼠李糖基团可以与GLUT1特异性相互作用。纳米探针被肿瘤摄取后，酚羟基的质子化将导致Fe^{3+}的释放，通过铁死亡/凋亡联合诱导肿瘤细胞死亡。同时，剩余的Fe（Ⅲ）-RH配合物在近红外激光照射下可作为光热治疗剂。

2.6 脂质体 脂质体是临床转化中最为成功的纳米药物，以Doxil、DaunoXome和Onivyde为代表的脂质体已在肿瘤治疗中得到广泛应用[119-122]。因此，开发新型脂质体设计对于扩宽剂型应用范围、提高药物治疗效果、攻克临床难治疾病具有重要作用[123]。例如，YU等[124]将大麻二酚和20（*S*）-原丙二醇共同加载于脂质体中，旨在二种中药活性成分可以起到协同抗肿瘤的效果。正十二烷基*β*-*D*-麦芽糖苷（Mal）在脂质体双层中的掺杂可以使葡萄糖残基锚定在脂质体表面上，赋予大麻二酚脂质体GLUT1靶向性。研究结果表明GLUT1靶向型CP脂质体具有良好的抗肿瘤功效和剂量依赖性，在良好的耐受性下实现了高肿瘤抑制率。

中药活性成分双氢青蒿素具有一定的抗肿瘤活性，可以作为过氧化氢的前体药物用于肿瘤治疗。但双氢青蒿素的溶解度低和靶向性差限制其在肿瘤治疗中的临床应用。因此，ZHANG等[125]构建了烷基糖苷修饰的双氢青蒿素脂质体，旨在提高双氢青蒿素的溶解度和靶向性。实验结果表明，烷基糖苷修饰脂质体的肿瘤靶向性（GLUT1）及抗肿瘤活性均有显著提高。

3 讨论与展望

目前的研究显示大多数化疗药物都存在溶解度低、靶向性差、容易耐药及不良反应大等缺点[126-129]。随着研究人员对肿瘤细胞Warburg效应机制的深入研究，与传统化疗药物相比，GLUT1靶向型中药活性成分纳米递送系统在肿瘤治疗具有许多明显的优势，如能够提高药物的溶解度、循环时间和生物利用度，提高靶向效率，减少不良反应[130]。有学者利用人参皂苷为膜材，对化疗药物紫杉醇和多西他赛进行负载，旨在提高化疗药物的递送效率[131-135]。实验结果显示相对于胆固醇脂质体而言，负载化疗药物的人参皂苷脂质体基于自身的GLUT1靶向性可以提高肿瘤细胞对化疗药物（紫杉醇和多西他赛）的摄取能力，靶向效率提高了2倍以上。

本文总结了基于Warburg效应的肿瘤异常糖代谢机制，以及用于肿瘤治疗的GLUT1靶向型中药活性成分纳米递送系统的最新进展。尽管基于GLUT1靶向型中药活性成分纳米递送系统在肿瘤治疗中取得了一系列进展，但大多数研究都集中在基础理论上，仅在动物模型中完成了验证，并没有进行临床试验。因此，基于GLUT1靶向型中药活性成分纳米递送系统可能会限制未来的大规模生产和临床应用。此外，为了解决未来GLUT1靶向型中药活性成分纳米递送系统临床转化面临的长期挑战，在设计GLUT1靶向型中药活性成分纳米递送系统时，应考虑成分、结构、形态、尺寸、表面改性和比表面积等重要因素[136-138]。

总体而言，GLUT1靶向型中药活性成分纳米递送系统为克服化疗药物的安全性和有效性差、无法靶向肿瘤细胞、循环时间短等缺点提供了新的解决

方案[139]。但GLUT1靶向型中药活性成分纳米递送系统临床转化的主要障碍除了临床前肿瘤模型不能模拟病人肿瘤组织复杂的病理特征、生产工艺、工业化生产、批次间质控等之外，还有基础研究科学家对临床试验的要求了解不足及临床医生未能及时掌握GLUT1靶向型中药活性成分纳米递送系统基础研发的最新研究进展。目前，GLUT1靶向型中药活性成分纳米递送系统从实验室基础研究走向临床应用是抗肿瘤纳米制剂研发中的关键问题。虽然GLUT1靶向型中药活性成分纳米递送系统临床前阶段的实验研究已取得突破性进展，但距实现有效临床治疗效果的核心目标仍相差甚远[140]。在实验室研发阶段，可对GLUT1靶向型中药活性成分纳米递送系统的制备过程实现优化，并进行重复性试验，但在产量放大阶段，应该确保GLUT1靶向型中药活性成分纳米递送系统各批次质量的一致性，并制定一套快速准确评估不同批次之间可重复性的方案。

因此，开发具有诊疗一体化的GLUT1靶向型中药活性成分纳米递送系统具有重要意义，可以使用多模态成像技术实时监测GLUT1靶向型中药活性成分纳米递送系统在肝脏和肾脏等器官中的清除。在此，本文系统总结了各种GLUT1靶向型中药活性成分纳米递送系统在肿瘤诊断与治疗中的应用。值得注意的是，GLUT1靶向型中药活性成分纳米递送系统可以通过结合GLUT1受体进而透过血脑屏障，这可能对于脑部肿瘤的靶向治疗提供新的策略。GLUT1靶向型中药活性成分纳米递送系统的发展不应局限于本文报道的纳米药物，其在未来将是一个关键的研究方向。此外，需要做大量工作来消除GLUT1靶向型中药活性成分纳米递送系统在肿瘤诊断与治疗临床应用的障碍。未来，GLUT1靶向型中药活性成分纳米递送系统可能会大规模应用于肿瘤的精准治疗。

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