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Multifunctional GQDs for receptor targeting, drug delivery, and bioimaging in pancreatic cancer

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Pancreatic cancer is a devastating disease with a low survival rate and limited treatment options. Graphene quantum dots (GQDs) have recently become popular as a promising platform for cancer diagnosis and treatment due to their exceptional physicochemical properties, such as biocompatibility, stability, and fluorescence. This review discusses the potential of multifunctional GQDs as a platform for receptor targeting, drug delivery, and bioimaging in pancreatic cancer. The current studies emphasized the ability of GQDs to selectively target pancreatic cancer cells by overexpressing binding receptors on the cell surface. Additionally, this review discussed the uses of GQDs as drug delivery vehicles for the controlled and targeted release of therapeutics for pancreatic cancer cells. Finally, the potential of GQDs as imaging agents for pancreatic cancer detection and monitoring has been discussed. Overall, multifunctional GQDs showed great promise as a versatile platform for the diagnosis and treatment of pancreatic cancer. Further investigation of multifunctional GQDs in terms of their potential and optimization in the context of pancreatic cancer therapy is needed.

1. Introduction

Pancreatic cancer, an extremely fatal condition, is frequently discovered in an advanced stage, which makes its treatment challenging.[1,2] Surgery, radiation therapy, chemotherapy, and targeted therapy are currently available treatments for pancreatic cancer.[3] The most effective treatment option is surgery for early-stage pancreatic cancer, which involves the removal of the tumor and the surrounding tissues. However, surgery is not always possible due to the location of the tumor or the patient's overall health.[4,5] Radiation treatment and chemotherapy are often used in combination with surgery or as a standalone treatment for advanced pancreatic cancer. Meanwhile, radiation treatment employs high-energy radiation to extinguish cancer cells, whereas chemotherapy uses drugs to eradicate cancer cells.[6,7] There are several types of pancreatic cancer, each with distinct characteristics and causes. The most common type of pancreatic cancer, accounting for about 95% of cases, is exocrine pancreatic cancer. It originates in the exocrine cells of the pancreas, which produce enzymes that aid in digestion. There are two main subtypes of exocrine pancreatic cancer. One is pancreatic ductal adenocarcinoma (PDAC), the most common subtype of exocrine pancreatic cancer which typically arises in the cells lining the pancreatic ducts and is often diagnosed at an advanced stage.[8] The other subtype is adenosquamous carcinoma which contains both exocrine glandular tissue and squamous epithelial tissue. It is relatively rare and tends to be more aggressive. The second type of pancreatic cancer is endocrine pancreatic cancer, which is also known as the neuroendocrine tumor. These tumors arise from the endocrine cells of the pancreas, which produce hormones that regulate blood sugar levels. They are generally less common and tend to grow more slowly than exocrine tumors. Neuroendocrine tumors can be further classified into functional and non-functional tumors based on whether they produce hormones that cause specific symptoms. The exact causes of pancreatic cancer are not always fully understood, but several risk factors have been identified such as age, tobacco use, family history and genetics, obesity, chronic pancreatitis, diabetes, diet, alcohol consumption, and occupational exposures.[9,10]

Targeted therapy is a newer treatment approach that uses drugs to specifically target cancer cells by blocking the proteins or pathways that drive their growth and survival. Some targeted therapies have been approved for use in pancreatic cancer, but they are not yet a standard treatment option.[11,12] Despite the advances in treatment, pancreatic cancer remains

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a challenging disease with a low survival rate. Early detection and diagnosis are critical for improving the outcomes, but there is currently no effective screening test for pancreatic cancer. Still, various research studies are ongoing to develop new treatments and improve outcomes for patients with this devastating disease.[13–16] Researchers are on the search for affordable sustainable sources of resources that are environmentally appropriate in order to manufacture new useful materials in light of the present biological and environmental challenges. The concepts of creating materials that are safe for patients and the environment are in line with the biocompatibility and low toxicity of GQDs. The long-term environmental effect may be reduced using GQD-based drug delivery systems that are tailored to metabolize or degrade into non-toxic components.[17] On the other hand, novel types of bioderived nanomaterials are reported for biomedical applications to treat a variety of ailments that impact both humans and animals.[18–20]

Also, GQDs are small graphene fragments with unique physicochemical properties, such as good biocompatibility, stability, and fluorescence, which make them better candidates for a wide range of biomedical applications such as drug delivery, bioimaging, biosensing, receptor drug targeting, antimicrobial activities, *etc.*[21–23]

As imaging agents, GQDs can be used for cancer detection and monitoring, drug delivery for targeted and controlled release of therapeutic agents, or as therapeutic agents themselves due to their ability to induce cytotoxicity in cancer cells without damaging healthy cells.[24] On the other hand, GQDs are precisely attached to cancer cells, targeted molecules, such as antibodies or peptides, or other disease biomarkers, to enable highly specific targeted diagnosis and treatment.[25,26] Moreover, GQDs have a high surface area to volume ratio, which permits them to interact with biological systems in unique ways, such as binding to proteins, nucleic acids, and lipids. These interactions can lead to potential applications in biosensing, biocatalysis, and gene editing.[27,28]

However, despite their promising potential, the use of GQDs in biomedical applications is still in its early stage, and more study is required to suitably comprehend their biological effects and the optimization of their performance in *in vitro* and *in vivo* studies. In this review article, an overview of the distinctive characteristics of GQDs has been explored, which make them a viable platform for drug delivery, bioimaging, biosensor, and other biomedical applications with the ability to completely change the practice of medicine.

2. Synthesis and various properties of multifunctional GQDs

There are different synthetic methods such as chemical vapor deposition, chemical exfoliation, electrochemical oxidation, microwave-assisted synthesis, *etc.* to synthesise graphene quantum dots (GQDs). In the process of producing GQDs, each technique has its own distinct importance, which may influence the final GQDs in terms of their form, size, surface modification, and other aspects (Table 1).[29–31]

The GQDs exhibit important properties that are suitable for various biomedical applications and are characterized by various modern techniques such as transmission electron microscopy (TEM), atomic force microscopy (AFM), dynamic light scattering (DLS), Fourier-transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), UV-vis absorption spectroscopy, Raman spectroscopy, fluorescence spectroscopy, *etc.*[40–42]

TEM,[43] DLS[44] and AFM[45] were used to establish the size, shape, and morphology of the GQDs, whereas XRD was utilized to identify the crystal structure of the GQDs.[46] FTIR and Raman spectroscopy techniques have been used to identify functional groups and confirm the presence of graphene-related structures,[47] respectively. The optical characteristics of GQDs have been determined using UV-Vis absorption spectroscopy, while fluorescence spectroscopy has been used to evaluate their fluorescence properties.[48,49]

To develop multifunctional GQDs, various functionalization methods could be employed, *i.e.*, surface modification with targeting molecules, such as antibodies or peptides, or conjugation with therapeutic agents or imaging dyes. The functionalization of GQDs can be achieved through various methods, such as chemical modification, covalent bonding, electrostatic interaction, or physical adsorption.[50] Xia *et al.* developed microRNA155 (miR), which was conjugated with graphene quantum dots (GQDs) on the surface of therapeutic monocytes as a novel approach to enhance immune treatment. Through surface-engineered monocyte immunotherapy, the TME was reversed by reprograming pro-tumor M2 TAMs into anti-tumor M1, greatly enhancing tumor elimination. The group concluded that surface-modified monocyte immunotherapy has been confirmed to be biocompatible and well adapted to intravenous delivery, demonstrating the expanded potentiality for solid tumor treatment (Fig. 1).[51]

Table 1 Different types of GQDs for various biomedical applications

S. no.	Type of GQD	Material used to develop	Method used	Biomedical application	Ref.
1	GQDs	Graphite rods	Electrochemical	Tumor detection	32
2	GQDs	Graphite powder	Hydrothermal	DNA nanosensor	33
3	RF-GQDs	Graphite and $K_2S_2O_8$	Electrochemical	Cellular imaging	34
4	F-GQDs	Fluorographene	Liquid exfoliation	MRI contrast agent	35
5	GQDs	Carbon fibre	Acidic exfoliation	*In vivo* biodistribution	36
6	B-GQDs	4-Vinylphenyl boronic acid and boric acid	Polymerization	MRI contrast agent	37
7	GQDs	Citric acid	Pyrolysis	Drug delivery system	38
8	FA-GQDs	Citric acid and folic acid	Pyrolysis	Photothermal therapy	39

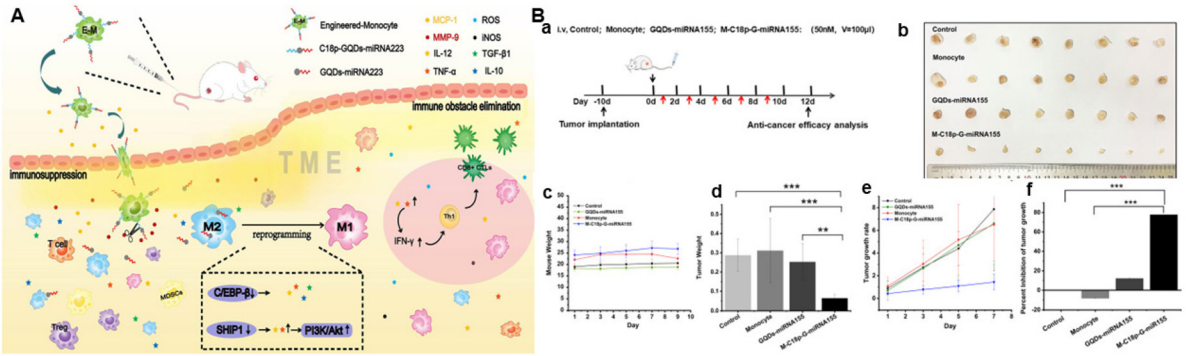

Fig. 1 (A) Illustration of graphene quantum dots paired with surface-engineered monocyte immunotherapy that is effective against solid tumor targets. (B) Analysis of the effectiveness of *in vivo* anticancer therapy: (a) a scheme showing BALB/c mice with 4T1 subcutaneous tumors being treated with the control, monocyte, GQDs-miRNA155, and M-C18p-G-miR155 at various day intervals, (b) photographs of the 4T1 subcutaneous tumors after the end of full treatments, and (c) weight change of 4T1 tumor-bearing mice injected with different treatments, (d) 4T1 subcutaneous tumor weight of each mouse in groups with the treatment of control, monocyte, GQDs-miRNA155 and M-C18p-G-miR155, respectively. Tumor growth rate (e) and tumor inhibition rate (f) calculations for each mouse in groups receiving various treatments. Reproduced under the Creative Commons licenses from ref. 51 with permission from Taylor and Francis, copyright 2023.

Overall, the synthesis and characterization of multifunctional GQDs is a critical step in their development for biomedical applications. By optimizing the synthesis and functionalization methods, GQDs can be tailored to meet the specific needs of a particular application, ultimately leading to the development of more effective diagnostic and therapeutic tools in medicine.

2.1. Methods for synthesizing GQDs with multifunctional properties

Various methods have been reported for synthesizing GQDs with multifunctional properties. These methods are typically used to introduce specific functionalities to GQDs, such as targeting moieties or therapeutic agents, to improve their performance in biomedical applications (Fig. 2). Chemical modification is one of the synthetic methods which involves the addition of functional groups to the surface of GQDs to endow them with specific properties. For example, carboxyl groups could be added to the surface of GQDs to increase their water solubility, while amine or thiol groups can be added to enable the attachment of targeting molecules or therapeutic agents.[52]

Besides this, covalent bonding involves the attachment of functional groups or targeting moieties directly to the surface of GQDs using chemical reactions. These methods could result in stable and specific conjugation but might require harsh reaction conditions that could damage GQDs.[53] The electrostatic interaction method involves the attachment of charged molecules to the surface of GQDs through electrostatic forces. This method is simple and does not require any harsh reaction conditions, but might result in non-specific binding.[54]

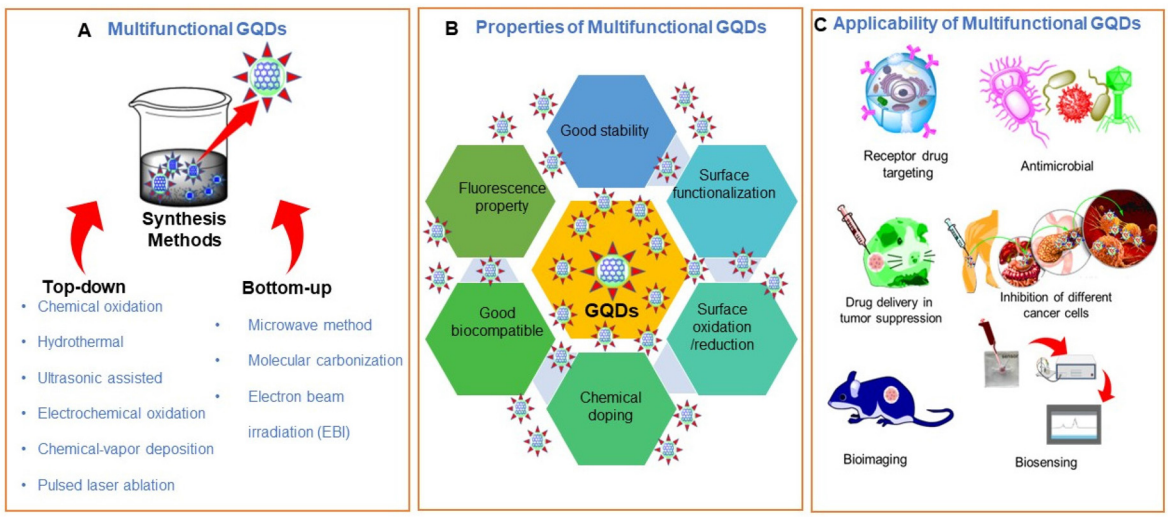

Fig. 2 Various methods to develop multifunctional GQDs. (A) Various routes of synthesis for the preparation of GQDs, (B) properties of multifunctional GQDs, and (C) a wide range of applications of multifunctional GQDs.

Physical adsorption involves attaching molecules to the surface of GQDs through interactions with π–π stacking or van der Waals forces. This method is simple and does not require chemical modification or covalent bonding, but may result in weak binding.[55] The one-pot synthesis method also involved the simultaneous synthesis and functionalization of GQDs in a single reaction. This method could result in GQDs with tailored properties but required careful optimization of the reaction conditions to ensure the achievement of the desired functionality.[56]

Moreover, the choice of the synthesis method will depend on the desired properties and intended applications of GQDs. By incorporating multifunctional properties into GQDs, they can be tailored to meet the specific needs of a particular application, ultimately leading to the development of more effective diagnostic and therapeutic tools in medicine.

2.2. Properties of GQDs for the treatment of pancreatic cancer

Treatment of pancreatic cancer may be one of the possible uses of graphene quantum dots (GQDs), which are tiny carbon-based materials with special features. The subsequent GQD characteristics may be important for the management of pancreatic cancer, even if research in this field is currently continuing and changing. Besides this, there have been various nanotechnological techniques reported for the cure and treatment of pancreatic cancer (Table 2).

2.2.1. Properties of GQDs to target ligands. Targeting ligands are often used to functionalize GQDs and imparted specific targeting properties, such as targeting specific cells or tissues in biomedical applications.[25] There are various targeting ligands that could be used to synthesize multifunctional GQDs. Antibodies are one of the targeting ligands that could

Table 2 Various reported nanotechnology systems for the imaging/diagnosis/detection of pancreatic cell lines and cancers

S. no.	Cell line/cancer/model	Type of nanocarrier/technique	Reported result	Ref.
1	Panc-1 (human pancreatic cancer cell line)	Human serum albumin (HSA)-coupled GQD NPs	GQDs had demonstrated exceptional bioimaging capabilities, and the addition of hyaluronic acid as a targeting moiety on HSA-NPs boosted the drug's capacity to combat the resilient pancreatic cancer cells.	57
2	Panc-1	Magnetic iron oxide nanoparticles with a superparamagnetic core are coupled with a positively charged drug erlotinib	Fe_3O_4 NPs showed magnetic activity, Au NCs exhibited red fluorescence properties, and erlotinib was used to target pancreatic cancer cells.	58
3	Human pancreatic cancer xenograft mouse model	Upconversion nanoparticles (UCNPs) with gadolinium ion doping, also known as active targeting UCNP-based micelles	Pancreatic cancer was effectively identified using magnetic resonance imaging and fluorescent PEGylated UCNPs coupled with the anti-human CD326 antibody. It has exceptional imaging sensitivity, the capacity to target tumors, and fewer systemic effects.	59
4	DNA derived from fecal samples taken from patients	Magnetic nanoprobe	Techniques could distinguish between patients with pancreatic cancer, benign illness, and healthy controls by detecting KRAS mutations with great sensitivity.	60
5	Panc-1 and in an animal model of pancreatic cancer	Mesothelin (MSLN)-targeted nano-immunoliposome	MRI capacity of the formulations has been demonstrated to be strong, and its targeted distribution in tumor cells has been much enhanced.	61
6	Panc-1	Iron oxide nanoparticles that have been bifunctionalized with amino and carboxylic acids and associated with antibodies (EPCAM: epithelial cell adhesion molecule) and rhodamine B isothiocyanate (RITC) enable MRI-fluorescent bimodal imaging.	Targeting capacity of the EPCAM antibody is provided by a protein produced on the surface of pancreatic epithelial cells.	62
7	Pancreatic cancer cells, MiaPaCa	Bioconjugated non-cadmium-based quantum dots (QDs) for pancreatic cancer	Early cancer detection is made possible by the conjugated QDs' efficient receptor-mediated absorption.	62
8	Subcutaneous inoculation into mice	Superparamagnetic iron oxide (SPIO)-labeled human pancreatic cancer cells	Pancreatic tumor xenograft's core primarily contained iron.	63
9	Engineered mouse models	Magnetofluorescent nanoparticles (NPs) coupled to plectin-1-targeted peptides (PTPs).	Precursor lesions and small pancreatic ductal adenocarcinoma were effectively identified.	64
10	Mouse models	Pancreatic acinar cell's normal bombesin (BN) receptors are the targets of NP conjugates.	MRI imaging of the pancreatic tumor has been improved by the conjugated NPs.	65
11	Tumor stroma from resected human pancreatic adenocarcinoma	Targeted PEGylated gold NPs with bioconjugates of the monoclonal F19 antibody as a labeling agent	Images clearly showed the differences between malignant and healthy pancreatic tissues, demonstrating the efficacy of the targeting capacity of PEGylated gold NPs–antibody bioconjugates.	66
12	Orthotopically xenografted human pancreatic cancer in nude mice.	Targeted NPs for the urokinase plasminogen activator receptor (uPAR)	Conjugated NPs can image uPAR-elevated pancreatic cancer lesions *in vivo* using optical and magnetic resonance techniques.	67

be used to direct GQDs to specific cells or tissues. For example, antibodies against specific receptors on cancer cells could be conjugated to GQDs to enable specific targeting and uptake by cancer cells.[25] Peptides could be useful as targeting ligands to enable specific binding to receptors or proteins on cell surfaces. For example, peptides that could bind to integrin receptors, which are overexpressed on cancer cells, could be conjugated to GQDs to enable specific targeting and enhanced uptake by cancer cells.[68]

Small molecules could also be used as targeting ligands to direct GQDs to specific cells or tissues. For example, small molecules that bound to specific receptors on cancer cells could be conjugated to GQDs to enable specific targeting.[69] So far, the targeting ligand will depend on the specific application and target of interest. By incorporating targeting ligands into GQDs, they could be tailored to bind specifically to the desired target, enabling more effective and targeted delivery of therapeutic agents or imaging dyes.

2.2.2. Drug loading capacity of GQDs. GQDs exhibit unique optical, electronic, and physical properties that are effective in a diversity of applications, including drug loading. The drug loading capacity of GQDs with multifunctional properties depends on various factors, including their size, surface properties, the type of drug being loaded, the method of synthesis, *etc*.[70] Studies have shown that GQDs could be synthesized with various functional groups on their surfaces, which could enhance their drug loading capacity. For example, GQDs could be functionalized with carboxylic acid or amine groups, which could provide a high density of reactive sites for drug conjugation.[71]

In addition to their functional groups, GQDs could also be made with a porous structure that provided a large surface area for drug adsorption or could be synthesized with magnetic properties that allowed for targeted drug delivery using magnetic fields.[72] The drug loading capacity of GQDs could also be influenced by the type of drug being loaded. It has been reported that hydrophobic drugs, such as paclitaxel and doxorubicin, could be effectively loaded onto GQDs due to their hydrophobic interactions with the graphene surface.[73] On the other hand, hydrophilic drugs might require additional functionalization or modification of GQD surfaces to facilitate their loading.[74]

Therefore, the drug loading capacity of GQDs with multifunctional properties could vary depending on several factors. However, with careful synthesis and functionalization, GQDs have the potential to be highly effective drug delivery carriers.

2.2.3. Imaging properties of GQDs. GQDs have unique electronic and optical properties that made them extremely appealing for imaging/bioimaging applications.[72,75] The synthesized GQDs with multifunctional properties have the potential to revolutionize imaging capabilities. In the case of fluorescence imaging, GQDs showed also excellent fluorescence properties. The synthesized GQDs with multifunctional properties could be designed to emit light at specific wavelengths, which could be used for imaging different types of cells or tissues.[76–79]

GQDs could be modified with magnetic materials, such as iron oxide, which made them highly useful for MRI applications. The synthesized GQDs with multifunctional properties could be designed to have both fluorescence and magnetic properties, which could be useful for both fluorescence and MRI imaging.[70] Also, GQDs have excellent photoacoustic properties with highly useful photoacoustic imaging applications. The synthesized GQDs with multifunctional properties could be designed to have both photoacoustic and fluorescence properties, which can be used for both photoacoustic and fluorescence imaging.[80]

While in biomedical imaging, GQDs showed excellent biocompatibility with high specificity in biomedical imaging applications. The synthesized GQDs with multifunctional properties could be designed to target specific cells or tissues for targeted biomedical imaging.[81] Overall, the synthesized GQDs with multifunctional properties have the potential to revolutionize imaging capabilities, with applications ranging from fluorescence imaging to biomedical imaging.

2.2.4. Other properties of GQDs to target pancreatic cancer cells. GQDs also have various properties to target pancreatic cancer cells in applications such as photothermal therapy (PTT), photodynamic therapy (PDT), radiotherapy, biosensing and detection, and theranostics. It has been reported that GQDs exhibit strong light-absorbing properties, which can be utilized for photothermal therapy (PTT). When exposed to near-infrared (NIR) light, GQDs have the ability to convert light energy into heat, effectively destroying cancer cells by increasing their temperature. Studies also described the applications of GQDs as photosensitizers in photodynamic therapy (PDT), which can generate reactive oxygen species (ROS) when exposed to light of specific wavelengths. ROS can induce apoptosis (programmed cell death) in cancer cells, helping to shrink tumors.[82]

Besides these uses, GQDs have been investigated for their potential to enhance the effectiveness of radiotherapy. They were incorporated into cancer cells which can enhance the absorption of ionizing radiation, leading to increased cancer cell death during radiotherapy sessions. Also, GQDs can be engineered to detect specific biomolecules associated with pancreatic cancer which can serve as biosensors for early diagnosis and monitoring disease progression. GQDs are also reported for theragnostic applications, combining therapy and diagnostics in a single platform. This approach allows the real-time monitoring of the treatment efficacy and adjustment of therapeutic strategies.[83]

3. Approaches to target receptors using GQDs in pancreatic cancer

Pancreatic cancer is an extremely hostile cancer that often has a poor prognosis. Various biomolecules and receptors play important roles in the progression and spread of pancreatic cancer. Some of the key receptors and biomolecules such as EGFR, HER2, integrins, MMPs, TGF-β, IGF-1R, *etc*. have been involved in pancreatic cancer.[84] These receptors and biomolecules are potential targets for the new therapeutic treatment of pancreatic cancer. Targeting these molecules could be more useful to inhibit tumor invasion, metastasis, and their growth, and in the enhanced efficacy of chemo- and radiation therapies.

There is evidence that graphene quantum dots (GQDs) have the potential to be used as tailored drug delivery systems in cancer treatment. Their capacity to target receptors overexpressed in pancreatic cancer cells, such as the epidermal growth factor receptor (EGFR), has established specific consideration.[85] One approach to target EGFR with GQDs involves the functionalization of GQDs with molecules that could bind specifically to EGFR receptors. Functionalized GQDs are reported with EGFR-specific aptamers in an *in vitro* experiment to target pancreatic cancer cells. Specifically, the aptamers on the surface of the GQDs enable them to bind EGFR receptors on the pancreatic cancer cells, leading to the internalization of the GQDs and the associated drug payload.[86]

It was also described that the usage of functionalized GQDs with folic acid to target pancreatic cancer cells that overexpressed folate receptors. These functionalized GQDs have the potential to specifically connect with the folate receptors found on pancreatic cancer cells, resulting in the internalization of the cells and the administration of drugs.[87] However, additional research is required to optimize the design and delivery of GQD-based therapeutics in pancreatic cancer.

3.1. Targeting receptors through GQDs

GQDs are reported to play important roles in cancer therapy and other biomedical applications. They could be functionalized with different moieties to enhance their targeting ability towards specific receptors, especially for pancreatic cancer.[88,89] Both passive targeting and active targeting *via* endocytosis are strategies used to enhance the delivery of GQDs into tumor tissues. Passive targeting leverages the EPR effect to achieve accumulation, while active targeting employs specific ligands to guide GQDs into tumor cells *via* endocytosis. These approaches hold promise for improving the efficacy and precision of cancer therapeutics and diagnostics (Fig. 3).[90]

One of the strategies for GQD design is to develop conjugates with different antibodies to target overexpressed receptors in pancreatic cancer such as EGFR and HER2. Antibody-conjugated GQDs can improve their specificity and efficacy to deliver anticancer drugs to cancer cells, reduce systemic toxicity, and enhance imaging sensitivity.[91]

GQDs can also be conjugated with peptides that bind specifically to pancreatic cancer cells to improve their targeting ability. Peptides such as RGD (arginine–glycine–aspartic acid)

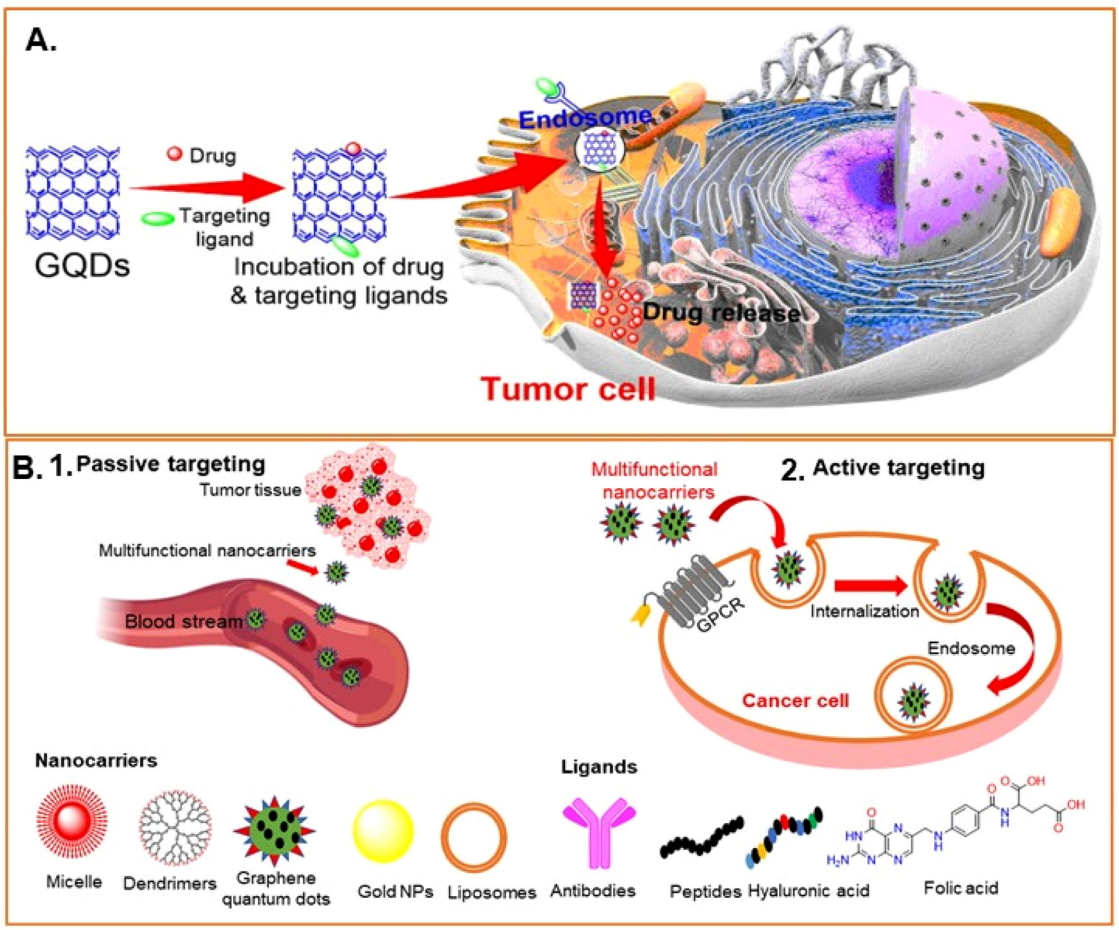

Fig. 3 GQDs and their role in the treatment of various solid tumor and cancers. (A) Targeted delivery of GQDs inside the tumor cells *via* endocytosis, (B1) passive targeting of GQDs into tumor tissues, and (B2) active targeting of GQDs *via* endocytosis.

can target integrins overexpressed in pancreatic cancer, while peptides such as AP1 and AP2 can bind to HER2 and EGFR, respectively.[92]

Surface modification with polyethylene glycol (PEG) means that PEGylation of GQDs can improve their biocompatibility, reduce their immunogenicity, and surge their flow time in blood circulation. PEGylation can also enhance their targeting ability towards cancer cells by reducing non-specific interactions with normal cells.[93] Yan *et al.* developed GQDs which were a great tool for multimodal, long-term, and fluorescence *in vivo* tumor bioimaging in a number of contexts. PEGylated nanoparticles of PEG nanocomposite systems with GQDs were used to make these GQDs and then they were delivered *in situ* utilizing a molecular technique that started from the bottom and worked its way up (Fig. 4).[94] Compared to regular GQDs, these GQDs showed 7–8 times greater tumor development and nearly four times longer blood circulation in an animal model. After accessible specificity adjustment, multifunctional NPs-GQDs-PEG provided targeted multimodal molecular imaging for a variety of tumor types in *in vitro* or *in vivo* studies. Highly photostable GQDs also allowed for the long-term observation of the *in vivo* local pharmacokinetics of NPs. They claimed that incorporating GQDs into PEGylated nanomedicine provides a novel method for GQDs to be used widely in *in vivo* biomedical applications (Fig. 5).[94]

On the other hand, coating GQDs with lipids or polymers could improve their stability, solubility, and targeting ability towards cancer cells. Lipid-coated GQDs can facilitate their uptake by cancer cells *via* endocytosis, while polymer-coated GQDs could improve their bioavailability and half-life.[95] Overall, GQDs functionalized with targeting moieties have the possibility of improving the clinical outcomes of pancreatic cancer therapy.

Antibody conjugated GQDs are also reported which target EphA2, a receptor tyrosine kinase overexpressed in pancreatic cancer cells. The study showed that EphA2-targeted GQDs could precisely bind to pancreatic cancer cells that induced apoptosis. The research group also demonstrated that the GQDs can be employed for precise imaging of pancreatic cancer cells.[96]

In addition to this, the effectiveness of targeting achieved by EGFR-targeted GQDs in pancreatic cancer cells was studied. GQDs were conjugated with an EGFR-specific antibody to demonstrate that EGFR-targeted GQDs can selectively bind to EGFR-overexpressing pancreatic cancer cells and inhibit their growth. The study also showed that EGFR-targeted GQDs can improve the efficiency of chemotherapeutic drugs by refining their intracellular delivery.[97]

The *in vivo* targeting effectiveness of PEGylated GQDs in a pancreatic cancer xenograft mouse model was also reported. Herein, the research group demonstrated that PEGylated GQDs

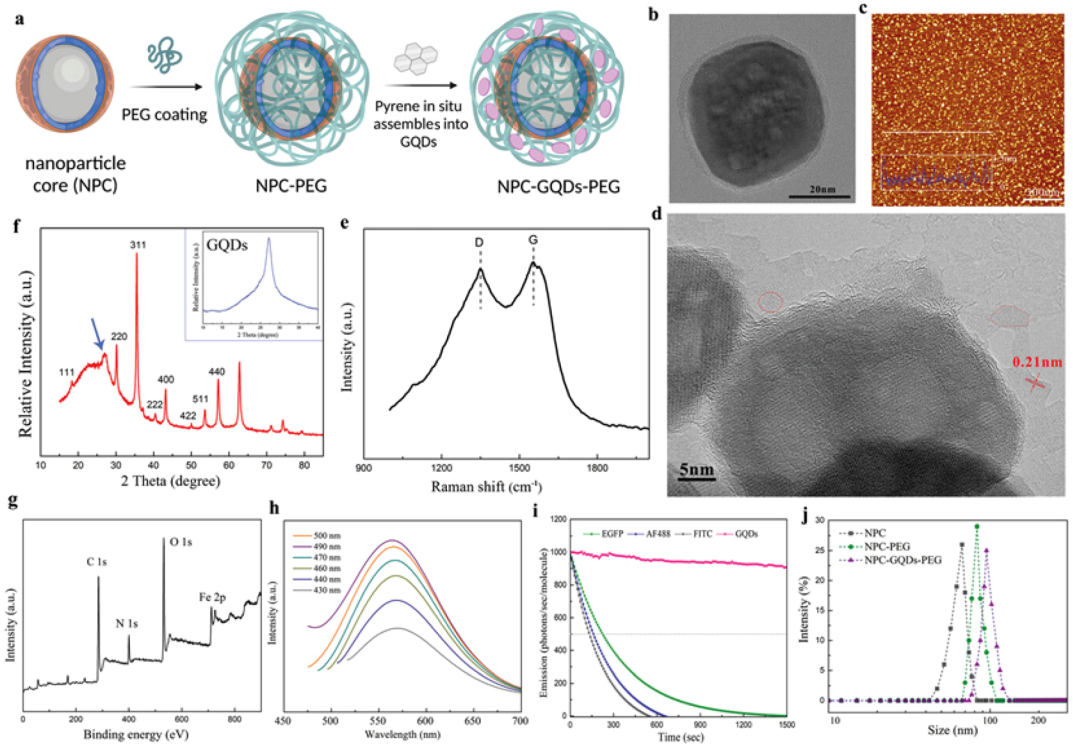

Fig. 4 Development and evaluation of NPC-GQDs-PEG nanoparticles. (a) Preparation of NPC-GQDs-PEG-based nanoparticles, (b) TEM image of the NPC core, (c) AFM image of pure GQDs, (d) HRTEM image of NPC-GQDs-PEG NPs, (e) Raman spectrum of NPC-GQDs-PEG, (f) XRD pattern of NPC-GQDs-PEG (inset: XRD pattern of pure GQDs), (g) survey XPS spectrum of NPC-GQDs-PEG, (h) PL spectra of NPC-GQDs-PEG excited at various wavelengths, (i) arc-lamp photobleaching curves of green-emitting NPC-GQDs-PEG, EGFP, Alexa Fluor 488 (AF488), and FITC dyes under constant arc-lamp illumination, and (j) hydrodynamic diameters of the NPs of various processes. Reproduced from ref. 94 with permission from Wiley-VCH, copyright 2023.

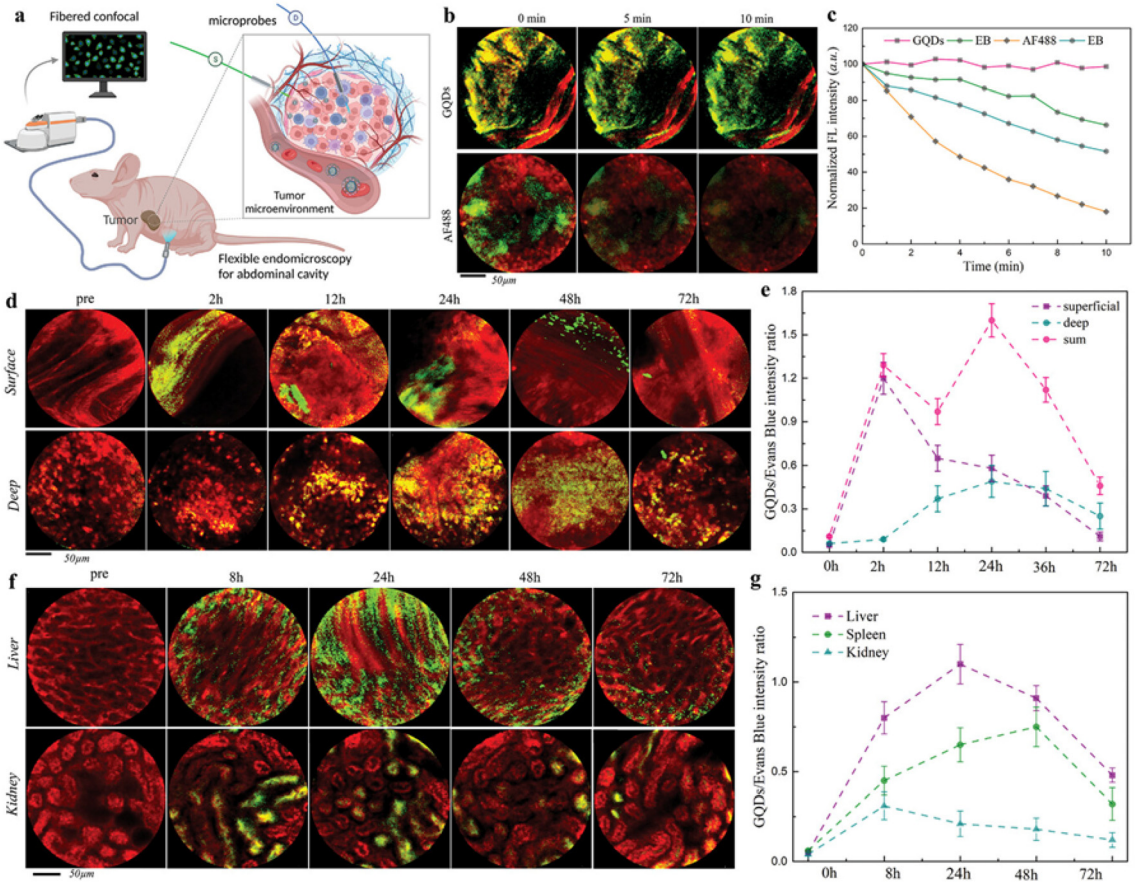

Fig. 5 Real-time and long-term monitoring of NPC-GQDs-PEG in local tissues. (a) Imaging of malignancies and large organs using fibered confocal fluorescence microscopy (FCFM) in the abdominal cavity. (b) An assessment of the photostability of NPC-GQDs-PEG/2-DG (green) and NPC-AF488-2-DG (green) in an *in vivo* MCF-7 tumor. The vascular contrast agent employed was Evans blue (red). (c) Measurement of the fluorescence intensity of the tumor using Evans blue (EB), AF488, and GQDs. (d) *In vivo* monitoring of probes' buildup, diffusion, and biodistribution in tumor tissues using FCFM. Green: NPC-GQDs-PEG/2-DG and red: EB. (e) Quantification of the fluorescence strength of NPC-GQDs-2-DG in superficial and deep tumor tissues at various time intervals (n = 4). (f) *In vivo* monitoring of the biodistribution and the metabolism of probes in the liver and kidneys using FCFM. (g) Quantification of the fluorescence intensity of NPC-GQDs-PEG/2-DG in the living tissues, spleen, and kidneys at different time points (n = 4). Reproduced from ref. 94 with permission from Wiley-VCH, copyright 2023.

can selectively accumulate in pancreatic tumors and improve the imaging sensitivity. This study also showed that PEGylated GQDs exhibit good biocompatibility and low toxicity, indicating their potential for clinical translation.[98] Perini *et al.* recognized the effects of GQDs combined with temozolomide and doxorubicin in a sophisticated 3D spheroid model of glioblastoma. They discovered that a critical element in the improvement of membrane penetrability on a 3D model increased the capacity of GQDs to collect and transform near-infrared light into heat. They recommended the combination of photothermal treatment (PTT) with chemotherapy at low dosages, which greatly increased the impact of anticancer medications by drastically reducing tumor viability and growth. Additionally, the release of ROS was enhanced with robust immune system passage towards irradiation cancer spheroids due to the increase in membrane permeability brought about by GQD-mediated PTT. They experimented that the enhancement in the membrane permeability might increase the effectiveness of anticancer medications against glioblastoma at subtherapeutic levels while decreasing the adverse effects and guiding immune responses (Fig. 6).[99]

In another study, a research group synthesized GQDs coated with polyethyleneimine (PEI) and conjugated them with peptide targeting neuropilin-1 (NRP-1), a protein overexpressed in pancreatic cancer cells. This study showed that the NRP-1-targeted GQDs could efficiently deliver siRNA targeting KRAS, a commonly mutated gene in pancreatic cancer, to pancreatic tumors in a mouse model. The group demonstrated that the KRAS-targeted GQDs could considerably slow down tumor development and increase mouse survival.[100] Altogether, these studies demonstrate that GQDs might be a suitable nanoplatform for pancreatic cancer-targeted drug delivery and imaging. The targeting efficiency of GQDs could be enhanced by conjugating with specific antibodies or peptides, or by modifying their surface with PEG or polymers. Further preclinical and clinical studies are required to adequately assess the effectiveness and safety of GQD-based therapies in pancreatic cancer.

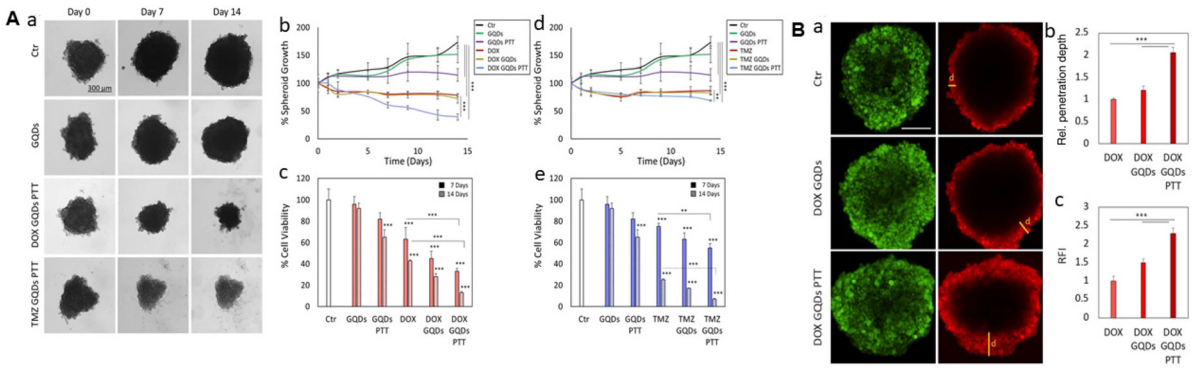

Fig. 6 (A) Impact of combining chemotherapy with GQD-mediated PTT on glioblastoma spheroid model tumors. (a) Bright field images of spheroids, (b) development of spheroids after the treatment with GQDs-PTT and DOX, (c) cell viability of spheroids, (d) development of the spheroids after the treatment with GQDs-PTT and TMZ, and (e) development of spheroids after various day intervals. (B) Penetration of DOX in the presence of GQDs-PPT. (a) Confocal microscopy images of spheroid cells labeled with calcein (left) and treated with DOX (red). (b) Dissemination of DOX inside the spheroids. (c) Fluorescence intensity of DOX inside the spheroids. Reproduced from ref. 99 with permission under the Creative Commons CC BY license from Springer Nature, copyright 2023.

4. Drug delivery using GQDs in pancreatic cancer

4.1. Enhanced drug delivery and DNA-damaging GQDs in tumors

Due to their distinctive physical and chemical characteristics, including the large surface area, biocompatibility, and photoluminescence, GQDs have demonstrated potential as drug delivery carriers for pancreatic cancer.[101,102] In a study, it was published that GQDs can efficiently deliver gemcitabine, a commonly used chemotherapy drug for pancreatic cancer, to pancreatic cancer cells. The study showed that GQD-mediated gemcitabine delivery could enhance the intracellular accumulation and cytotoxicity of the drug, leading to improved anticancer efficacy.[103] Qi *et al.* produced GQDs that specifically damaged the DNA of cancer cells to slow down tumor development. Nucleus-targeting TAT peptides (TAT-NGs) were used to create modified amine-functionalized GQDs, and were additionally combined with folic acid (FA)-adapted PEG by a disulfide linkage to target cancer cells. The resulting FAPEG-TNGs demonstrated excellent biocompatibility, cancer cell targeting and nucleus uptake which could adsorb on DNA by electrostatic interactions, causing DNA damage, upregulating apoptosis-related proteins, and eventually stopping the proliferation of cancer cells. This research provided a reasonable GQD design that promoted DNA damage to achieve excellent therapeutic efficacy, crucial to a unique chemotherapeutic approach for targeted tumor treatment (Fig. 7).[104]

4.2. Drug delivery using Glucosamine-coupled GQDs

To test the ability of GQDs to target and kill breast cancer cells that have overexpressed GlcN receptors, Ghanbari *et al.* developed a targeted, traceable, and pH-responsive drug delivery system using the hydrophobic anticancer substance curcumin (Cur) loaded onto glucosamine (GlcN)-coupled graphene quantum dots (GQDs). These environment friendly and simple oxidizing techniques were used to prepare biocompatible photoluminescent GQDs from graphene oxide. The GQDs and Cur/GlcN-GQDs were characterized structurally and spectrally. The GQDs had less than 10 layers and had diameters between 20 and 30 nm. The Cur-loaded nanocarrier also exhibited sustained release and pH-sensitive behavior, with total drug release values of 37% at pH 5.5 and 17% at pH 7.4 after 150 hours. *In vitro* cellular uptake studies utilizing fluorescence microscopy and flow cytometry indicated higher fluorescence for the targeted nanocarrier *versus* MCF-7 cells compared to the non-targeted one because of increased cellular internalization *via* GlcN receptor-mediated endocytosis. Furthermore, the results of the MTT experiment showed that the bare nanocarriers were harmless, with cell survival levels above 94% even at concentrations as high as 50 g^{-1}, in contrast to the Cur/GlcN-GQDs, which displayed much higher cytotoxicity against MCF-7 cells than Cur/GQDs. The research group concluded that the delivery capacity of this complex multifunctional nano-assembly was higher for breast cancer cells (Fig. 8).[105]

4.3. Targeted GQDs for efficient delivery and cancer suppression

In a published study, GQDs were synthesized and coated with polyethylenimine (PEI) and conjugated with folic acid, a ligand that could target the folate receptor overexpressed in pancreatic cancer cells. The study showed that the folic acid-targeted GQDs can efficiently deliver doxorubicin, a potent chemotherapy drug, to pancreatic cancer cells and enhance their cytotoxicity.[106] GQDs coated with chitosan could efficiently deliver siRNA-targeting KRAS to pancreatic cancer cells. The study showed that KRAS-targeted GQDs could significantly suppress the progress of pancreatic cancer cells and sensitized them to chemotherapy drugs.[103] Another research group synthesized GQDs coated with PEI and conjugated with siRNA-targeting survivin, a protein overexpressed in pancreatic cancer cells. The study showed that the survivin-targeted GQDs could

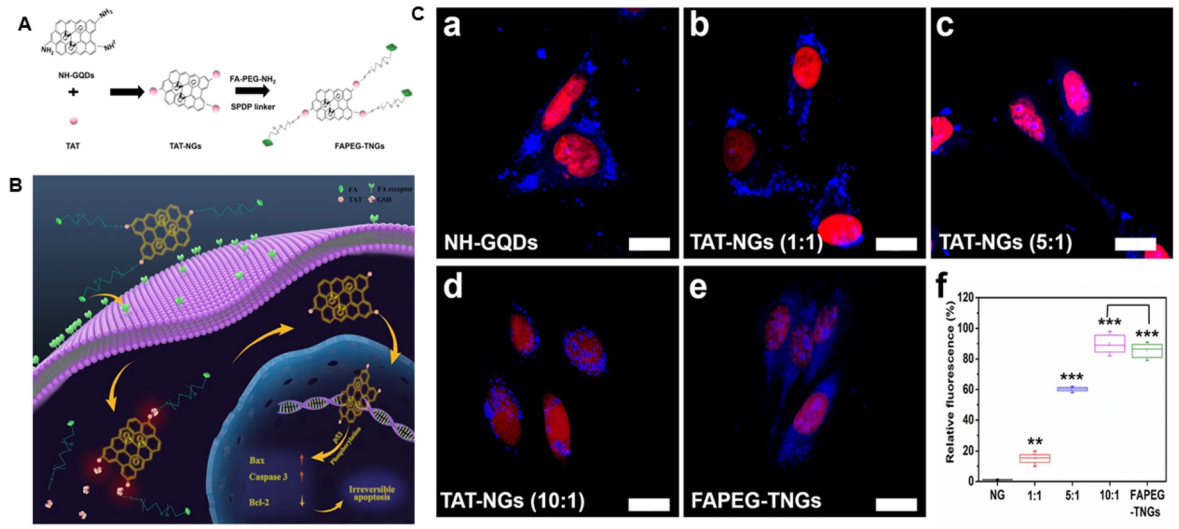

Fig. 7 (A) Illustration of the preparation of FAPEG-TNGs, (B) the FAPEG-TNG therapeutic mechanism in the cancer cell and (C) fluorescence images of HeLa cells nurtured with NH-GQD derivatives: (a) NH-GQDs, (b) TAT-NGs (1 : 1), (c) TAT-NGs (5 : 1), (d) TAT-NGs (10 : 1), and (e) FAPEG-TNGs. (f) The endonuclear fluorescence strength of TAT-NGs and FAPEG-TNGs in comparison with that of NH-GQDs (the images are overlaid with the blue color of the NH-GQD derivatives and the red color of tainted nuclei with 7-aminoactinomycin D (7-AAD, component B). Reproduced under the Creative Commons CC BY license from ref. 104 with permission from Springer Nature, copyright 2021.

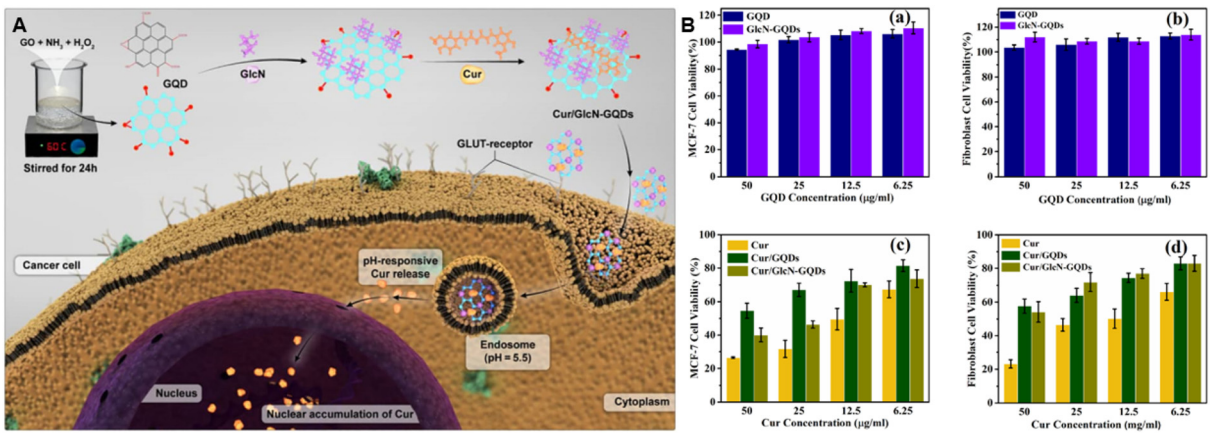

Fig. 8 (A) A summary of adaptable and pH-sensitive GQDs for improved curcumin delivery in the targeting of breast cancer. (B) *In vitro* cytotoxicity of GQDs and GlcN-GQDs following the MTT assay: (a) MCF-7 cells and (b) fibroblast normal cells. The anticancer activity of Cur/GlcN-GQDs, Cur/GQDs, and free Cur following the MTT assay: (c) MCF-7 cells and (d) fibroblast normal cells. Reproduced with permission from ref. 105 permission from Elsevier, copyright 2021.

efficiently deliver siRNA to pancreatic cancer cells and induce apoptosis.[107] Further preclinical and clinical studies are still warranted to fully estimate the safety and effectiveness of GQD-based therapies in pancreatic cancer.

Therefore, the treatment options for pancreatic cancer, a tumor with a poor prognosis and high aggressiveness, are limited and typically involve a combination of surgery, radiation therapy, and chemotherapy. Chemotherapy is often used as an adjuvant therapy to reduce the risk of recurrence after surgery or as a palliative therapy to alleviate symptoms and prolong survival conditions at an advanced disease level.[108] There are various commonly used chemotherapeutic agents that are reported in the treatment of pancreatic cancer such as gemcitabine (a nucleoside analogue), FOLFIRINOX (a combination of four chemotherapeutic agents: 5-fluorouracil (5-FU), leucovorin, irinotecan, and oxaliplatin), nab-paclitaxel (a protein-bound form of paclitaxel), cisplatin (a platinum-based chemotherapy drug), capecitabine (an oral chemotherapy drug), *etc*. Other chemotherapy drugs that could also be used in the treatment of pancreatic cancer are docetaxel, paclitaxel, mitomycin C, and topotecan. The choice of this chemotherapy regimen will depend on the stage of the disease, the patient's overall health, and other factors, and should be made in consultation with a medical professional.[109–111]

On the other hand, in covalent bonding, drugs are chemically attached to GQDs through covalent bonds. This method provides a more stable and controlled drug loading compared to physical adsorption. However, it requires more complex synthetic procedures and can potentially alter the structure and properties of GQDs. The drugs can be covalently bonded to the surface of GQDs using various coupling agents such as carbodiimides, succinimides, or diazonium salts.[102,112] In another article published by Li *et al.* described a high-performance nanosystem built on GQDs that has been shown to upload a cyclic (RGDfC) peptide to overcome PDT resistance in cancer. The as-prepared cRGD-GQDs showed excellent pH stability, high singlet oxygen quantum yield ($\Phi\Delta$ = 0.95), and strong biocompatibility. The ability of c(RGDfC) and integrin v3 to specifically bind one another allowed the cRGD-GQDs to favourably cluster in tumor cells and continually produce significant quantities of ROS. In particular, following repeated PDT treatment assisted by cRGD-GQDs, several PDT resistance-related components, such as the pump protein ABCG2 and antioxidant proteins *i.e.*, Nrf2, HO-1, and NQO-1, persisted at a low level. However, after repeated treatment of PDT with free GQDs, a considerable elevation of these variables could be seen. As a result, cRGD-GQDs demonstrated potent anticancer PDT effects both *in vivo* and *in vitro* by blocking the cancer cell routes for survival. They came to the conclusion that the study offered a potentially attractive therapeutic method for overcoming the developed PDT resistance and had significant implications for the development of future PDT medicines (Fig. 9).[113]

4.4. Comparative analysis of different GQD types for drug delivery

The potential of GQDs as a drug delivery platform for the treatment of pancreatic cancer has also been the subject of several research studies. Additionally, several *in vitro* and *in vivo* experiments have shown that GQD–drug complexes are effective at inhibiting pancreatic cancer cells and reducing the tumor size.[114] Sawy and coworkers created two different kinds of GQDs known as GQDs1 and GQDs2, characterized and overloaded them with the chemotherapeutic drug doxorubicin (DOX), and contrasted them with other carbon nanomaterials (CNMs) under similar conditions. The effects of the shape, size, and surface charge of the produced CNMs on the efficiency of the DOX loading and emission as well as cytotoxicity against MCF-7 cells were investigated. Additionally, the biosafety of the produced GQDs was assessed *in vitro* using human WI-38 cells and *in vivo* using healthy female Wistar rats at low and high doses of 5 and 20 mg kg^{-1}.[115]

According to the study results, GO nanosheets had the maximum DOX loading capacity of 2.85 mg mg^{-1} and GQDs1 had the highest release rate of 78.1%. The *in vitro* cytotoxicity study revealed that GQDs1 had the smallest spherical

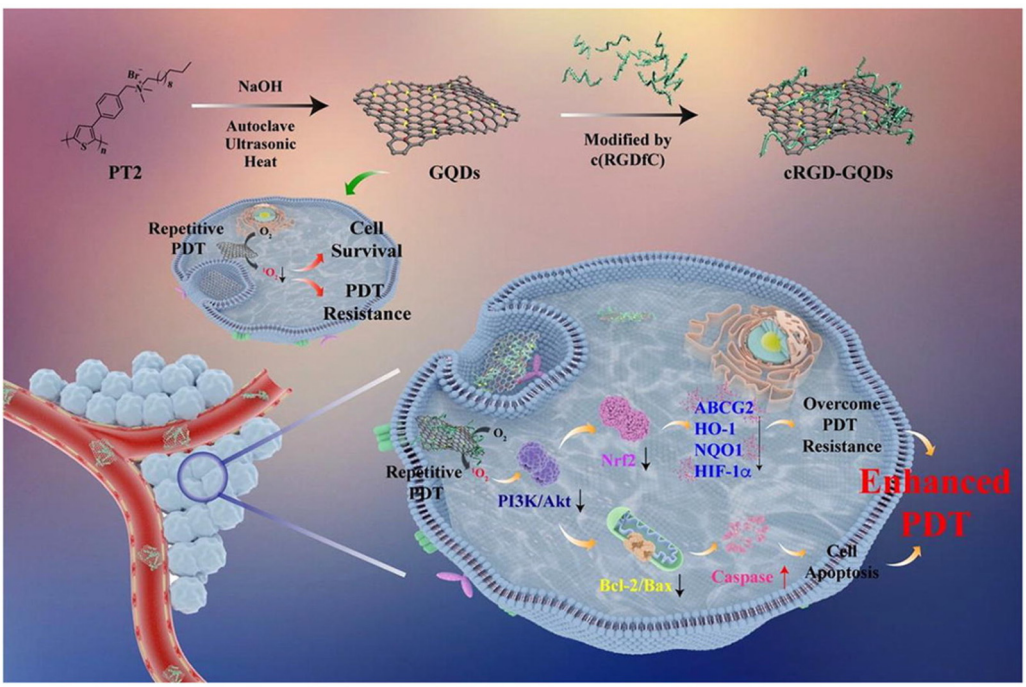

Fig. 9 An illustration of the pleiotropic process behind the improved PDT caused by cRGD-GQDs. Reproduced from ref. 113 with permission from Elsevier, copyright 2021. A very effective nanosystem built on GQDs that has been developed to upload a cyclic (RGDfC) peptide to overcome PDT resistance in cancer. The cRGD-GQDs have exceptional biocompatibility, a high singlet oxygen quantum yield, and great pH stability as they were initially synthesized. The ability of c(RGDfC) and integrin v3 to specifically bind one another allowed the cRGD-GQDs to effectively aggregate in tumor cells and continually produce large quantities of ROS. The cRGD-GQDs demonstrated potent anticancer PDT effects both *in vivo* and *in vitro* by impeding the cancer cells' survival pathways.

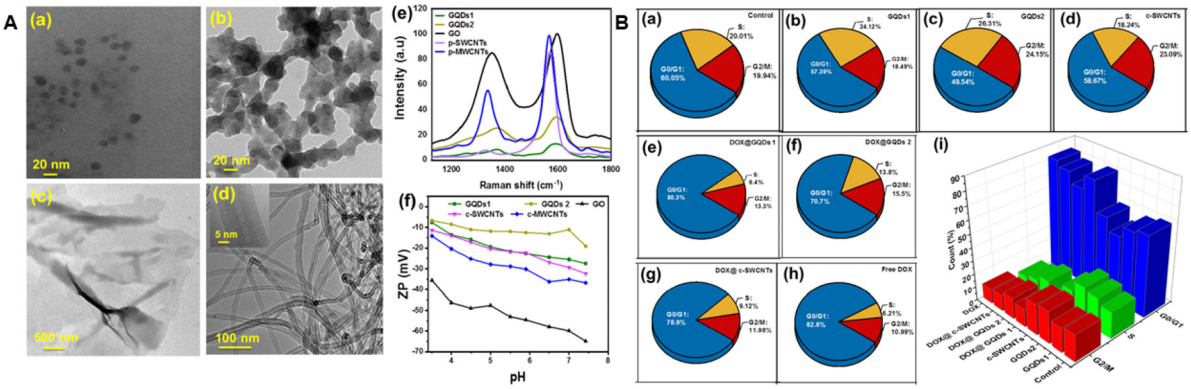

Fig. 10 (A) TEM images of (a), (b), (c), and (d) of the prepared GQDs1, GQDs2, GO, and MWCNTs, respectively. (e) Raman spectra of various CNMs. (f) Zeta potentials of GQDs1, GQDs2, GO, c-SWCNTs, and c-MWCNTs at various pH values. (B) (a–h) The effect of numerous formulations, CNMs, GQDs1, GQDs2, c-SWCNTs, free DOX, and their equivalent DOX@CNMs on the sequence of MCF-7 cells upon 48 h of treatment and (i) comparative 3D plot of the growth phases of control and treated cells. Reproduced from ref. 115 with permission from Elsevier, copyright 2021.

nanomaterial among the CNMs, which was the most effective in delivering DOX to the cells and inhibiting their proliferation. With regard to biosafety, all CNMs—aside from GQDs2—exhibited no discernible cytotoxicity against WI-38. Additionally, analysis of the kidneys and livers of treated rats using haematological, biochemical, and histological methods confirmed the excellent biosafety level. The group provided fresh perspectives on first-principles calculations by looking at the DOX adsorption on GO and GQDs. According to the calculations, DOX molecules were about equally adsorbed on both nanoforms; however, the flaky nature of GO monolayers enabled the creation of sandwich-like structures, which provided greater loading capacity particles than GQDs (Fig. 10).[115]

Another research group investigated and reported the efficacy of doxorubicin-loaded GQDs in the inhibition of pancreatic cancer cells (PANC-1 cells) in *in vitro* studies. The results showed that the GQD–doxorubicin complex had higher cytotoxicity against PANC-1 cells compared to the free doxorubicin, and the complex also induced apoptosis (programmed cell death) in cancer cells. These studies demonstrated the potential of GQDs as a successful method for delivering drugs to treat pancreatic cancer, and highlighted the importance of further research in this area. However, it is important to note that to assess the long-term effectiveness and safety, additional studies are required for GQD-based drug delivery systems in humans, and optimization of their pharmacokinetics and biodistribution in *in vivo* studies.[116]

5. Bioimaging using GQDs in pancreatic cancer

Bioimaging with graphene quantum dots (GQDs) has shown great potential in detecting and imaging cancer cells, including pancreatic cancer cells. GQDs are nanoscale materials with unique optical and electrical properties, which make them excellent imaging agents.[117] In pancreatic cancer, GQDs have been used for both *in vitro* and *in vivo* imaging studies. *In vitro* studies have shown that GQDs could selectively target pancreatic cancer cells and provide high-resolution imaging of their morphology and metabolic activity. It also has been used to label pancreatic cancer cells for fluorescence imaging and tracking.[118]

It has been reported that silibinin has a variety of therapeutic applications, including anticancer, antioxidant, hypocholesterolaemia, cardioprotective, neuroprotective, and hepatoprotective effects. However, due to its low oral bioavailability and the lack of *in vitro–in vivo* biological connection, it has only limited clinical applications. Takke and Shende developed and described magnetic GQD nanocomposites for silibinin administration with a focus on kidney cancer therapy and effective central composite design. The impact of silibinin, polyvinyl alcohol (PVA), and polylactic-*co*-glycolic acid (PLGA) composition on the mean particle size and encapsulation competency was investigated. The features of the generated magnetic graphene nanocomposites with silibinin magnetic nanoparticles showed particle sizes below 300 nm, good encapsulation effectiveness (81.27%), and increasing *in vitro* drug release that was demonstrated over time. According to *in vitro* cellular uptake experiments with kidney cancer cell line (A-498) samples, the magnetic graphene quantum dot nanocomposites demonstrated superior cellular absorption of silibinin and cytotoxicity than graphene quantum dots. The *in vivo* pharmacokinetic research showed a significant increase in drug bioavailability with increased mean residence length due to extended exposure to systemic circulation. As a result, silibinin administration by monodisperse magnetic graphene quantum dot nanocomposites against the kidney cancer cell line A-498 has been thought to be an intriguing option for the treatment of cancer (Fig. 11A).[119]

Lin *et al.* synthesized graphene quantum dots (N-GQDs) doped with nitrogen using the traditional hydrothermal process. To develop PEG:b-PEI@N-GQDs (P@N-GQDs), polyethylene glycol (PEG)-branched polyethylenimine (b-PEI) was

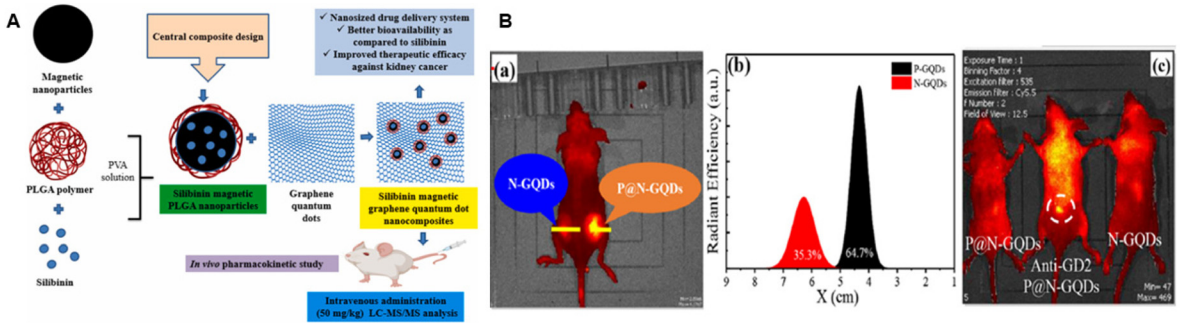

Fig. 11 (A) An illustration of monodisperse magnetographene quantum dot nanocomposites for silibinin delivery. Reproduced from ref. 119 with permission from Elsevier, copyright 2021. (B) *In vivo* imaging system (IVIS) spectra of (a) the subcutaneous tissue injection of N-GQDs and P@N-GQDs; (b) the yellow linear signal scanning in (a) shown as a relative ratio; (c) *in vivo* fluorescence emission (Ex: 535 nm/Em: Cy5.5) of the encouraged tumor organ in nude mice with Ab-GD2@P@N-GQD injection, which were separated into N-GQDs, P@N-GQDs and Ab-GD2@P@N-GQDs (anti-GQDs). Reproduced from ref. 120 with permission from Elsevier, copyright 2022.

further coated on the N-GQDs. In order to develop Ab-GD2@P@N-GQDs, the P@N-GQDs were coupled with an anti-GD2 antibody and visualized using an *in vivo* imaging system (IVIS). The fluorescent markers' physical makeup, optical characteristics, and *in vivo* imaging capabilities were investigated. The P@N-GQDs were found to have an irregular circular form with a diameter of 10.6 ± 1.7 nm. The P@N-GQDs' PL emission was increased from 450 to 550 nm. The signal of P@N-GQDs was increased to 1.83 times that of N-GQDs *in vivo*, improving their visibility in the IVIS spectrum as well. The Ab-GD2-P@N-GQDs accumulated in cancer cells, and the dissected tumor's highest fluorescence intensity was 6.72×10^7. The research group successfully recommended the probe as a treatment for neuroblastoma and noted its significant potential as a gene carrier (Fig. 11B).[120]

GQDs may be helpful for non-invasive imaging of pancreatic cancers in animal models, according to *in vivo* research. It has been used to label pancreatic cancer cells in mice, allowing for real-time visualization of tumor growth and metastasis.[26] GQDs have also been used for imaging pancreatic tumors in zebrafish models, providing high-resolution images of tumor morphology and progression.[121]

Also, GQDs exhibit high brightness, photostability, biocompatibility, small size, and versatility, making them an attractive option for bioimaging applications under both *in vitro* and *in vivo* conditions. Their unique properties make them excellent imaging agents for cancer detection and monitoring, including pancreatic cancer.[122,123] Further research is needed to optimize their use and evaluate their potential for clinical applications.

6. Current challenges and future directions

While GQD-based therapies hold great promise for increasing pancreatic cancer diagnosis and treatment, several challenges and future directions must be addressed to realize their full potential. One significant challenge is the need to optimize the properties of GQDs for specific applications (Fig. 12). For example, researchers must carefully select the size, surface chemistry, and targeting ligands of GQDs to ensure optimal tumor penetration, drug delivery, and imaging sensitivity. This requires a detailed understanding of the biological and physicochemical factors that influence GQD performance, as well as the ability to tailor their properties to the specific needs of individual patients.

Another challenge is to ensure the safety and efficacy of GQD-based therapies. While GQDs have shown promise in preclinical studies, their long-term safety and toxicity in humans are still largely unknown. Researchers must conduct rigorous safety and toxicity studies to identify potential adverse effects and determine appropriate dosing strategies. Additionally, reliable methods should be developed for monitoring the biodistribution and pharmacokinetics of GQDs to ensure their appropriate metabolism and clearance from the body.

It is anticipated that several strategies will be used, including the use of biomass, the combination of various hybridization states (sp, sp^2, and sp^3), synthesis pathways, functionalization, heteroatoms, or even novel carbon forms. All of these advancements are strongly tied to our transdisciplinary knowledge; technological progress which may lead us to a new age of materials synthesis and transformation, with a particular focus on environmentally benign methods of producing these materials. Furthermore, it is crucial to note that theoretical studies are required to accomplish this aim due to their vital role in determining the structures, electron mobility, functionality, and reactivity of carbon surfaces.

Another emerging trend is the functionalization of carbon-based materials, which allows for the customization of the surface chemistry needed for a particular application. It is important to note that the uniformity of the biomolecule immobilization process is a significant difficulty that might have an impact on how the target biomolecules interact with carbon-based substances. Achieving this aim might constitute a milestone since it could make it easier to build tiny devices. Combining diverse carbon-based materials with dimensionalities in synthetic procedures is not an easy task.

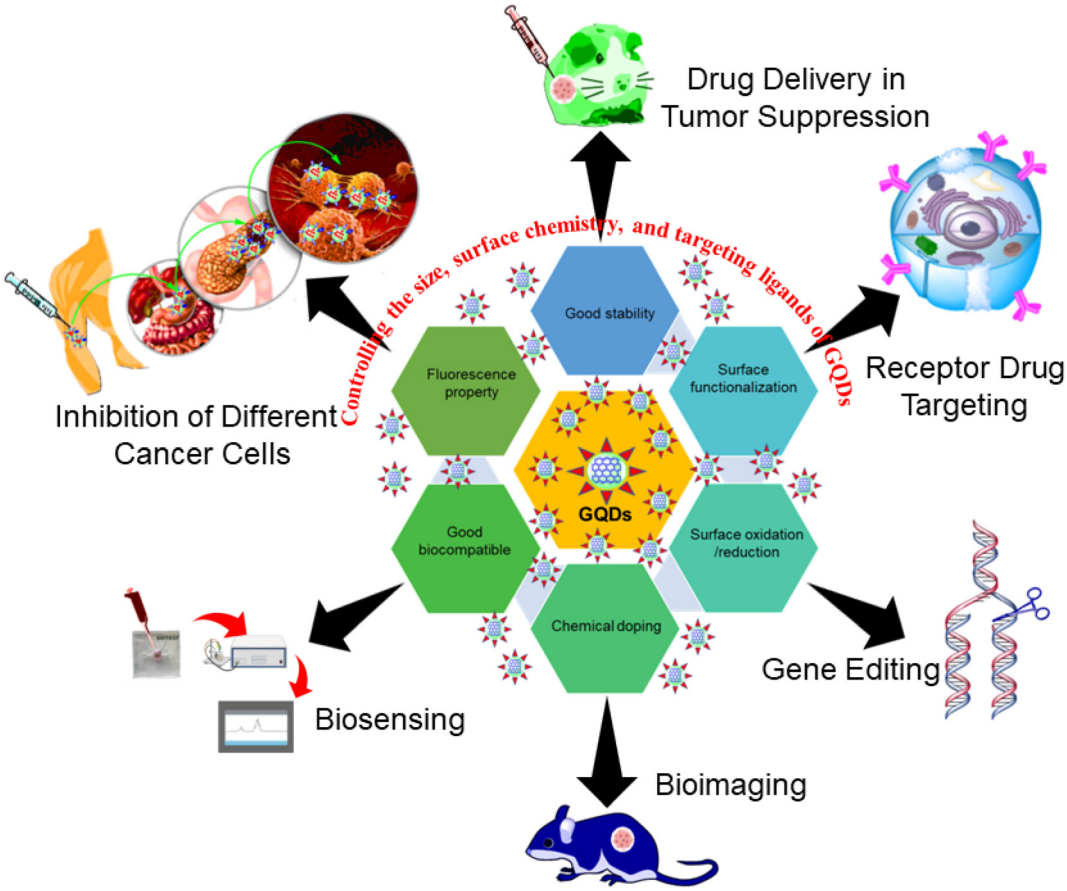

Fig. 12 Graphene quantum dots (GQDs) with tremendous potential in various biomedical applications due to their unique properties.

Future directions for GQD-based therapies in pancreatic cancer include the development of more effective targeting strategies, such as the use of combination therapies that target multiple biomarkers on cancer cells. Additionally, researchers may explore the use of GQDs for other applications, such as photothermal therapy and gene editing, which may offer additional avenues for enhancing pancreatic cancer detection and therapy.

Despite the fact that GQD-based treatments have a lot of potential for enhancing pancreatic cancer detection and therapy, overcoming the obstacles and considering new possibilities are essential to reach their full potential. Continued research and development in this field may ultimately lead to new and more effective treatments for this devastating disease.

7. Conclusion

Nanoscale carbon particles such as graphene quantum dots (GQDs) exhibit unique optical, electrical, and mechanical properties that make them attractive candidates for use in a wide range of biomedical applications. Researchers have recently looked into how multifunctional GQDs might be useful in pancreatic cancer detection and treatment. GQDs may be functionalized with fluorescent dyes and tumor-targeting ligands to provide extremely accurate and targeted imaging agents for the detection of pancreatic cancer. These agents could be useful for visualizing tumors in real time, allowing for more accurate diagnosis and surgical removal of the cancerous tissue. In addition to imaging, GQDs could also be useful for drug delivery. By functionalizing GQDs with targeted cancer-killing drugs to the respective ligands, researchers have demonstrated the ability to deliver drugs directly to pancreatic cancer cells, reducing harm to healthy tissues and increasing the effectiveness of treatment. Furthermore, GQDs could be useful in combination with other therapies, such as radiation and chemotherapy, to enhance their effectiveness *via* sensitization of cancer cells, making them more susceptible to these treatments. In this review article, GQDs with multifunctional properties as a promising tool for increasing pancreatic cancer detection and treatment have been discussed. Further research is needed to optimize and validate their properties and to ensure that GQDs are safe and effective.

Conflicts of interest

The authors have declared no conflicts of interest.

Acknowledgements

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