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RISE OF 2D MATERIALS TECHNOLOGY AND ITS POTENTIAL IN THE CANCER TREATMENT

Joshua Anthony Vomo[1] * and Milly Gladys Iteriteka[2]

[1]Department of Pharmacology, Raghavendra Institute of Pharmaceutical Education and Research, K.R. Palli Cross, Anantapur, Chiyyedu, Andhra Pradesh-515721-India.
[2]Department of industrial Pharmacy, Raghavendra Institute of Pharmaceutical Education and Research, K.R. Palli Cross, Anantapur, Chiyyedu, Andhra Pradesh-515721-India.

***Corresponding Author: Joshua Anthony Vomo**
Department of Pharmacology, Raghavendra Institute of Pharmaceutical Education and Research, K.R. Palli Cross, Anantapur, Chiyyedu, Andhra Pradesh-515721-India.

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ABSTRACT
The technology of 2D nanomaterials has gained importance and research interest in the pharmaceutical field due to its therapeutic value in various areas. 2D nanomaterials have attracted interest in biomedicine in areas such as biosensor, drug carrier and nanomedicine. In the treatment and diagnosis of cancer, 2D nanomaterials are used as a novel technology with high efficacy. 2D nanomaterials are used in the production of biosensors based on biomarkers, which are very effective compared to conventional biosensors. 2D nanomaterials are used in drug delivery as nanocarriers and are more effective due to their biocompatibility and biodegradability. 2D nanomaterials are used in novel anticancer drugs such as photothermal therapy, photodynamic therapy and combined cancer therapy, which has been shown to be effective and less harmful in various studies. In this review, we focus on the emerging 2D drug technology and its potential anti-cancer effects.

KEYWORDS: *2D nanomaterials, photothermal therapy, anticancer therapy, nanocarrier and 2D biosensors*.

1. INTRODUCTION

Cancer is one of the biggest public health problems and it is predicted that the number of cancer cases will increase by more than 20 million new cases per year by 2025.[1] According to GLOBOCAN, 9.7 million cancer deaths are expected in 2020.[1] Breast cancer, colorectal cancer, prostate cancer and lung cancer are the most commonly diagnosed cancers in Europe.[2] Lung cancer remains the leading cause of cancer incidence and death worldwide.[3]

Increasing knowledge of molecular and tumor biology has significantly changed the paradigms of cancer treatment over the last 15 years.[4] Clinical cancer therapies such as chemotherapy, surgery and radiotherapy have an unsatisfactory therapeutic effect as they inevitably damage healthy cells, are inefficient and can lead to relapse.[5] Recently, harmless tumor therapies with low damage to normal cells and high curative efficacy have been developed based on multifunctional nanomaterials for the diagnosis, imaging and treatment of cancer.[6] New technologies such as photothermal therapy are gaining ground in the fight against cancer. Conventional cancer treatments such as chemotherapy, surgery and radiotherapy often damage healthy cells, are less effective and can lead to relapse.[6] Non-invasive therapies with multifunctional nanomaterials show high efficacy with minimal damage. Photothermal therapy is a promising replacement for conventional cancer treatments. Photothermal therapy (PTT), in which near-infrared light is converted into heat to ablate tumor cells, has proven to be a promising alternative. 2D nanomaterials improve PTT due to their strong absorption in the near infrared and are therefore suitable for cancer theranostics.[7] However, the assessment of long-term biological safety remains a challenge. Combining PTT with chemotherapy or radiotherapy iproves treatment efficacy and reduces systemic toxicity.[7]

Recent advances in 2D nanomaterials have revolutionized cancer treatment and they offer targeted drug delivery, improved imaging and increased therapeutic efficacy.[8] These materials, such as graphene and transition metal dichalcogenides, offer a large surface area and unique properties that pave the way for more precise and effective cancer therapies.[9] 2D nanomaterials are characterized in cancer treatment by their large surface area, excellent biocompatibility and unique optical properties.[10] They enhance photodynamic and photothermal therapies, improve the precision of drug delivery and serve as sensitive biosensors.[11] Their versatility and efficiency make them ideal for targeted cancer therapies and diagnostic applications. 2D nanomaterials have significantly improved electrochemical biosensors for cancer diagnosis. These materials, such as graphene and its derivatives, enable highly sensitive detection of cancer biomarkers in various clinical samples.[11] 2D nanomaterials as biosensors, including nucleic acids, proteins and small molecules, enable accurate early cancer detection and valuable prognostic insights that improve therapeutic strategies.[12]

In drug delivery, 2D nanomaterials as nanocarriers are characterised by their stability, free flow in blood vessels and efficient entry into cells.[13] 2D materials improve nanocarriers with large surface areas, high drug loading and biocompatibility.[14] Their unique properties overcome the limitations of conventional systems and improve the efficacy of chemotherapy.[14]

2. METHODOLOGY

The methodology employed in the literature review aimed to comprehensively capture the relevant research on 2D nanomedicine used in cancer treatment. This was achieved through a meticulous approach that utilized several databases and specific keywords, along with clearly defined inclusion and exclusion criteria.

The search encompassed multiple databases, including PubMed, Scopus, Web of Science, and Google Scholar, to ensure a broad and diverse collection of relevant literature. A combination of keywords, such as "2D materials," "Anticancer therapy," "photothermal therapy," "biosensor," "Drug delivery," and "exfoliation," was used to capture all relevant literature. Boolean operators (AND, OR) were employed to refine the search and ensure that all pertinent studies were considered.

The selection process involved an initial screening of titles and abstracts based on inclusion and exclusion criteria, followed by a review of full-text articles for detailed analysis. This two-step process ensured that only studies that met the criteria for relevance were considered in the review.

Each selected study was critically analysed to extract data on 2D nanomaterials used in cancer therapy. This analysis considered the study design, sample size, methodology, key findings, and limitations. The critical appraisal of the literature helped to understand the robustness and applicability of the findings.

The literature was organized thematically or methodically, depending on the type and variety of findings. This organization helped to identify patterns, trends and gaps in the existing research.

3. CURRENT PROGRESSIVE OF 2D NANOMATERIALS

Two-dimensional (2D) nanomaterials technology have gained significance and research interested in pharmaceutical field due to therapeutic value in the various.[15] 2D nanomaterials have sparked interest in biomedicine filed in area such as biosensor, drug carrier and drug. In 2004, Andre Geim and Konstantin Novoselov were credited with discovering graphene, the first 2D material, and were awarded the Nobel Prize in Physics in 2010 for their ground-breaking work.[16] Graphene was the first 'modern' 2D nanomaterial to be isolated. Since then, hundreds of other 2D nanomaterials with a wide range of properties have been reported.[16] 2D materials are newly developed nanomaterials with atomic-scale thickness, large specific surface area, and distinct physicochemical properties.[17] They've been used in a wide range of applications and research areas, including energy storage, optoelectronics, biomedicine, drug delivery, and bio sensing.[17]

2D materials obtained by stripping exhibit unique physical, optoelectronic, and biological properties.[18] These materials, consisting of a single atom or a few atoms thick, exhibit excellent photoelectric, physicochemical, and biological properties.[18] These properties have attracted the attention of scientists in physics, chemistry, biomedicine, materials science, and nanotechnology.[19] They exhibit excellent electrical properties under the quantum-limited effect, leading to the development of electronic devices, such as field-effect transistors and logic devices.[19] Additionally, two-dimensional materials are widely used in photoelectric devices, flexible sensors, new energy sources, photocatalysis, and biomedicine owing to their mechanical properties and high specific surface area.[20] Their surface-based nature allows for interactions with biological receptors or biomolecules, making them ideal for high-sensitivity biosensors.[21] 2D materials significantly improve biosensor system performance and promote biosensor research.[21] 2D materials show promise in clinical medicine, particularly in fluorescence imaging, drug delivery, photodynamic therapy, and tissue regeneration therapy, in addition to their bio transducer applications.[22] Research on 2D materials has made significant progress, but there are still many problems to be solved, owing to increasing demand and the rapid development of science and technology.[23]

4. SYNTHESIS OF 2D NANOMATERIALS

4.1. Exfoliation

In synthesis of the 2D materials there are two main types of exfoliation namely as Mechanical and liquid exfoliation.[24] Mechanical exfoliation, invented by Novoselov and Geim in 2004, is a popular method for synthesizing 2D nanomaterials because of its versatility and low cost.[25] It involves using scotch tape to exfoliate an atomic layer of thick graphene from bulk graphite mesas, followed by the deposition of the exfoliated layers on the substrate.[26]

Liquid exfoliation is a top-down method that uses sonication to exfoliate bulk layered materials into 2D nanomaterials that are then dispersed in liquid solvents.[27] This process used low-power sonication to create atomically thin sheets and various 2D materials have been synthesized using solvent exfoliation processes, yielding 5-20 layers of nanomaterials that are homogeneously dispersed in a solvent.[28] The quality of the dispersion was controlled by the sonication time and centrifugation rate. However, the process is limited to producing nanostructures approximately 1µm in size.[28]

4.2 Chemical vapour Deposition

Chemical vapor deposition (CVD) is a high-temperature chemical synthesis process that deposits desired materials on substrates.[29] They have been used to synthesize thin-film coatings of various materials, including metals, semiconductors, and insulators.[29] CVD was not recognized as a method for 2-D nanostructure synthesis until studies demonstrated the synthesis of large-scale monolayer graphene on Cu foil by CVD under conditions of flowing methane at 1000 °C.[30] The synthesis of graphene on other transition metals using the CVD of hydrocarbons has been discussed in several recent reports[31] and CVD has also been applied to the synthesis of large-scale homogeneous 2-D transition metal dichalcogenides (TMDC) and boron nitride nanosheets.[32]

5. 2D NANOMATERIALS BIOSENSORS FOR CANCER DIAGNOSIS

In diagnosis of cancer in the patient, cancer biomarker used in diagnosis and prognosis of cancer.[33] Biosensors based on biomarkers are widely used for the laboratory analysis of the chemical and biological targets of cancer.[34] In recent years, 2D nanomaterials have advanced the technology of electrochemical biosensors and improved the performance of biosensors used in the diagnosis of cancer.[35]

In recent years, the emerging concepts in biosensors systems and the translation of these concepts into clinical trials have driven the development of 2D nanomaterial-based sensors for disease-agnostic applications.[36] In particular, 2D nanomaterials have achieved enormous applications for constructing electrochemical biosensors platforms to realize highly sensitive detection of cancer biomarkers present at ultra-low levels in a small number of diverse clinical samples.[37] The cancer bio- markers can be classified into different types, including embryonic antigen, carbohydrate antigen, and enzymatic tumour markers.[37]

Qualitative and quantitative analyses of cancer markers are of great clinical significance, as they provide the basis for the early detection or diagnosis of primary cancer, cancer classification, prognosis, and therapeutic guidelines.[38] The recent progress in the preparation and electrochemical biosensors applications of 2D nanomaterials for cancer detection, on graphene, graphene-related nanomaterials such as graphene oxide (GO) and reduced GO, and graphene-like nanomaterials.[39]

2D nanomaterial biosensors used in the diagnosis of cancer can be categorized as nucleic acid biosensors, protein biosensors, and small-molecule biosensors.[40] Nucleic acid biosensors use DNA and microRNA as biomarkers for the detection of cancer at an early stage, and it has been reported that metastatic tumor cells circulate in the blood and DNA is free in the blood because of lysis, thus making it easy to detect cancer.[40] Nucleic acids are very effective with a rapid response and sensitivity in the detection of nucleic acids from tumor cells.[40] Protein biosensors are used for early diagnosis of cancer and in response to cancer treatment also protein biosensors detect tumor biomarkers such as α-fetoprotein, carcinoembryonic antigen, squamous cell carcinoma antigen, and prostate-specific antigen.[40] Small-molecule biosensors use reactive oxygen and nitrogen species, which are important messengers for cellular signals. Elevated levels of reactive oxygen species and reactive nitrogen species are observed in cancer; therefore, they are very important in the diagnosis of cancer.[41]

6. 2D NANOCARRIER IN DRUG DELIVERY

Nanocarriers are nanomaterials that have a size of hundreds of manometers and possess the ability to load drugs and other biomedical agents.[42] For nanocarriers to be good, they should be stable and have free flow in the blood vessels that can easily enter into the cell via phagocytosis and be finally expelled from the cell.[42] The excellent physicochemical properties of 2D materials enable them to match well with their practical biomedical applications for instance, large surface areas are induced by their unique ultrathin planar structures, which facilitate high drug loading efficiency and are essential for the design of nanocarrier systems.[43] For a prospective nanocarrier, high stability in the bloodstream, high loading capability, and amphiphilic surface state are necessary. In this section, we focus on the synthesis and catalog of relevant nanocarriers based on emerging 2D materials.[44]

Nanocarriers that incorporate molecules to target cancer cells during therapeutic and diagnostic applications have been regarded as a ‘‘magic bullet.” ,this theranostic strategy avoids the disadvantages of conventional chemotherapy, such as ineffective drug access to target tumors, poor bioavailability, unfavorable biodistribution, and multidrug resistance these enhancements can remarkably improve the chemotherapy performance.[45]

In recent development of 2D nanocarriers research reports in the biomedical application classified by 2D material system, including graphene, transition metal dichalcogenides (TMDs), group-VA semiconductors, transition metal carbides (MXenes), graphitic carbon nitride (g-C3N4), and hexagonal boron nitride (h-BN).[46]

The physicochemical properties of 2D materials enable them to match well with practical biomedical applications for instance, large surface areas are induced by their unique ultrathin planar structures, which facilitate high drug loading efficiency, high biocompatibility and biodegradability.[46]

Compared to conventional drug delivery systems, such as solid lipids and polymers, these 2D materials possess many advantages, such as abundant family members, excellent inherent properties, and good biocompatibility.[47] Although many exciting 2D material based biomedical applications have been demonstrated, several vital issues and challenges still hinder their clinical application.[48] Although substantial progress has been made to evaluate biocompatibility, including cytotoxicity, solubility, and degradation in vitro and in vivo, the most important issues for biomedical clinical applications, the long-term biosafety and bioactivity of 2D materials, have not been comprehensively assessed.[49]

7. 2D MATERIALS IN CANCER TREATMENT

Clinical cancer treatments including chemotherapy[50], surgery[51], and radiotherapy have unsatisfactory therapeutic effect, such as inevitable damage to healthy cells, low efficiency, and possible recurrence so, it is necessary to exploit non-invasive tumour therapy approaches.[52] Recently, harmless tumour therapies with little damage to normal cells and high curative efficacy based on multifunctional nanomaterials have been rapidly developed in diagnosis, imaging, and treatment of cancers. In the development of the anticancer treatment there is rise of new technology such as photothermal that is a promising replacement for traditional cancer treatments.[53]

Emerging photo-thermal therapy (PTT) employs photothermal agents (PTAs) to convert Near-infrared light into hyperthermia for tumour cells ablation, which possess typical features of minimal invasiveness to normal tissues, non-invasiveness, mitigated side effects, and strong anti-tumour capability.[54] The mechanistic studies of PTT confirmed that the irreversible cell death can cause rapidly due to vessel formation and protein destruction when the tumour tissues are heated to temperature above 41 °C.[55] The prerequisite for PTT is high penetration into tumour buried deep in biological tissue and Near-infrared (NIR) light is the major laser for PTT applications due to its less absorption and scattering in biological tissues and higher energy of photons relative to UV light.[56]

The unique optical a properties of 2D nanomaterials can be harnessed for photothermal therapy.[57] Furthermore, by integrating 2D nanomaterials with other functional nanoparticles or utilizing their inherent physical properties, 2D nanomaterials may also be engineered as nanoprobes for multimodal imaging of tumors.[57] Moreover, many types of 2D nanomaterials typically exhibit strong absorbance of near-infrared (NIR) light, making them useful candidates in the photothermal therapy (PTT) of cancer and considering these exceptional characteristics, 2D nanomaterials have been shown to be interesting nanoplatforms for various cancer theranostic applications.[57]

The advent of graphene and its promising applications in various fields have led researchers to explore the applications and related properties of other types of 2D nanomaterials, such as transition metal dichalcogenides (TMDs), transition metal carbides, nitrides and carbonitrides (MXenes), black phosphorus nanosheets layered double hydroxides (LDHs), 2D metal–organic frameworks (MOFs),] Pd nanosheets, hexagonal boron nitride (hBN) nanosheets, antimonene (AM) nanosheets, and 2D boron (B) nanosheets.[58]

The sensitivity of oxygen-enriched cells to chemotherapy are higher than hypoxic cells, while the sensitivity to PTT are reversed.[59] Hence, when combining PTT with chemotherapy, hyperthermia is capable of improving tumour sensitivity to anticancer drugs and the uptake rates of drugs, suppressing drug resistance, and increasing drug accumulation in tumour tissues, which are responsible for enhancing the therapeutic effect of chemotherapy.[59] Besides, these two therapies could function synergistically, giving higher therapeutic efficacy.[60] Anticancer drugs and photosensitizers could also be loaded onto these 2D Photodynamic therapy (PDT) nanomaterials to achieve PTT chemotherapy or PTT-PDT synergistic treatment of tumours, thereby significantly improving the therapeutic efficacy of cancer[61]. Additionally, due to their strong X-ray attenuation capability to sensitize RT, Pd-based nanosheets could achieve dual-modal PA/CT-imaging-guided PTT-RT synergistic therapy of cancer.[62]

8. CONCLUSION

2D nanomaterial technology have gained significance and research interested in pharmaceutical field due to therapeutic value in the various.2D nanomaterials have sparked interest in biomedicine filed in area such as biosensor, drug carrier and nanomedicine. In the treatment and diagnosis of cancer 2D nanomaterials emerging as novel technology with high efficacy and low harm. Despite the 2D nanomaterials proved to be effective in drug delivery as nanocarrier due to their biocompatibility and biodegradation, and used photothermal therapy in the treatment of the cancer still biosafety and toxicology of the 2D nanomaterials is uncertain. Further research is needed to determine the biosafety and toxicology of 2D nanomaterials.

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