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GRAPHENE AS CARRIER/NANO CARRIER FOR DRUG DELIVERY SYSTEM

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ABSTRACT
Graphene, a two-dimensional carbon material, has emerged as a promising candidate for drug delivery systems due to its unique properties. Graphene has a high surface area, excellent mechanical strength, and good biocompatibility, making it an attractive platform for delivering therapeutic agents. In recent years, extensive research has been conducted to explore the use of graphene as a carrier for drug delivery systems for improving the efficacy and specificity of drugs, while reducing their toxicity. Various strategies have been employed to optimize drug loading and release from graphene as a carrier for drug delivery systems. Surface modification, functionalization, and encapsulation are some of the techniques that have been used to enhance the drug delivery efficiency of graphene. These techniques have resulted in increased drug loading capacity, improved release profiles, and enhanced targeting capabilities. graphene as a carrier for drug delivery systems have demonstrated significant potential in preclinical studies. These systems have shown improved pharmacokinetics, bioavailability, and targeted delivery compared to conventional drug delivery systems. Moreover, graphene has the potential to act as a biosensor, allowing for real-time monitoring of drug delivery. Despite its many advantages, the large-scale production, biocompatibility, and safety of graphene as a carrier for drug delivery systems are still major challenges. The biocompatibility of graphene needs to be carefully evaluated to ensure its safety for human use. The high cost of graphene production and the need for reproducible synthesis methods are additional obstacles that must be overcome.

KEYWORDS: Graphene, Drugdelivery, Biocompatibility, Surfacemodification, Functionalization, Encapsulation, Pharmacokinetics, Targeted delivery, Biosensor, Biocompatibility, Safety, Production, Efficacy, Specificity, Carbon material, Two-dimensional, High surfacearea, Mechanical strength, Bioavailability, Real-time monitoring, Reproducibility, Optimization, Efficiency etc.

1. INTRODUCTION
Graphene has gained a lot of attention in the field of drug delivery due to its unique properties like high surface area, mechanical strength, and high conductivity.[1] These properties have led to the development of a wide range of graphene as a carrier for drug delivery systems that have shown promising results.[1]

One of the most significant advantages of using graphene as a drug carrier is its ability to cross biological barriers such as the blood-brain barrier, which is a major challenge in drug delivery.[1] Graphene can also be functionalized with various molecules to enhance its biocompatibility and target specific cells or tissues.[1]

Graphene as a carrier for drug delivery systems have been shown to have several advantages over traditional drug delivery systems, including improved drug stability, increased drug solubility, and enhanced drug bioavailability.[1]

Graphene-based carriers can also be easily modified to control drug release rates, which can improve the efficacy of the delivered drug and reduce side effects.[2]

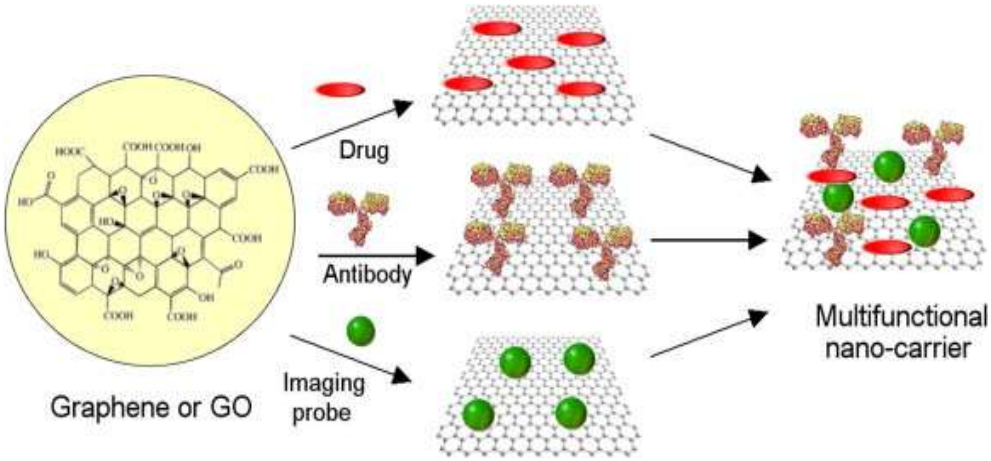

Fig. 1: Graphen or GO as a drug carrier.

Graphene has been explored as a carrier for various types of drugs, including small molecules, proteins, nucleic acids, and antibodies. One of the most promising applications of graphene as a carrier for drug delivery systems is in cancer therapy.[3]

Graphene-based carriers have been shown to effectively target cancer cells and deliver therapeutic agents directly to the tumor site, minimizing damage to healthy tissues. In addition, graphene can also enhance the efficacy of chemotherapeutic drugs by increasing their solubility and bioavailability.[3]

Graphene-based carriers have also been studied for the delivery of nucleic acid-based therapies, such as gene therapy and RNA interference (RNAi).[3] Graphene can protect the nucleic acids from degradation and enable their efficient delivery to target cells.[3]

Graphene oxide (GO) and reduced graphene oxide (rGO) are two of the most commonly used forms of graphene in drug delivery applications.[3] These materials can be functionalized with various molecules such as polyethylene glycol (PEG) or antibodies to enhance their biocompatibility and targeting ability.[3]

One of the challenges in using graphene as a carrier for drug delivery systems is ensuring their safety and biocompatibility.[4] While graphene has been shown to be non-toxic, concerns remain regarding its potential to induce inflammation and immune response in the body.[4] Therefore, further studies are needed to fully understand the safety and biocompatibility of graphene as a carrier for drug delivery systems.[4] Overall, graphene as a carrier for drug delivery systems have shown great potential in improving drug delivery efficiency and efficacy, and ongoing research in this field is likely to lead to the development of new and innovative drug delivery systems in the future.[4]

This review paper aims to provide an overview of the current status of graphene base drug delivery systems.[4]

1.1 Graphene as a drug carrier

Graphene is a two-dimensional material that consists of a single layer of carbon atoms arranged in a hexagonal lattice.[22] Due to its unique structure, graphene has high surface area, mechanical strength, and high conductivity, which make it an ideal candidate for drug delivery.[22]

2. Various type of graphene

2.1 Graphene oxide (GO): GO is a highly oxidized form of graphene, containing numerous oxygen functional groups such as hydroxyl, carboxyl, and epoxy groups. Its high surface area and biocompatibility make it a suitable material for drug delivery systems.[18]

Graphene oxide (GO) is a derivative of graphene, a two-dimensional material composed of a single layer of carbon atoms arranged in a hexagonal lattice. GO is created by oxidizing graphene, resulting in the addition of oxygen-containing functional groups such as hydroxyl, carboxyl, and epoxy groups to the graphene lattic.[18]

Fig. 2.1: Graphene oxide.

In addition to drug delivery applications, GO has been studied for its antimicrobial properties. Studies have shown that GO can inhibit the growth of various types of bacteria, making it a promising material for developing

antibacterial coatings and wound dressings.[19] Moreover, GO has also been explored for use in energy storage applications, such as in supercapacitors and batteries, due to its high surface area and excellent electrical conductivity.[19] GO-based materials have shown promising results in improving the performance and energy density of these devices.[19] However, the potential toxicity of GO remains a concern, and further research is needed to fully understand the safety of GO and its derivatives. Nonetheless, GO and its derivatives continue to be a subject of intense research, with numerous applications being explored in various fields.[19]

GO has several unique properties that make it attractive for a wide range of applications, including drug delivery, energy storage, and sensors.[20] GO has a large surface area, high mechanical strength, and excellent electrical conductivity, making it a versatile material for various applications.[20]

In drug delivery applications, GO has been extensively studied as a carrier for various types of drugs, including small molecules, proteins, nucleic acids, and antibodies.[20] GO can protect drugs from degradation and improve their solubility and bioavailability, resulting in enhanced therapeutic efficacy.[20]

2.2Reduced graphene oxide (rGO): rGO is obtained by reducing graphene oxide, which restores the sp2 carbon-carbon bonds.[6] rGO has a higher conductivity and mechanical strength than GO and has been used in drug delivery systems due to its good biocompatibility.[6]

Reduced graphene oxide (rGO) is a form of graphene oxide (GO) that has been reduced to remove most of the oxygen-containing functional groups.[6] The reduction process can be achieved through various methods, including thermal annealing, chemical reduction, or electrochemical reduction.[6]

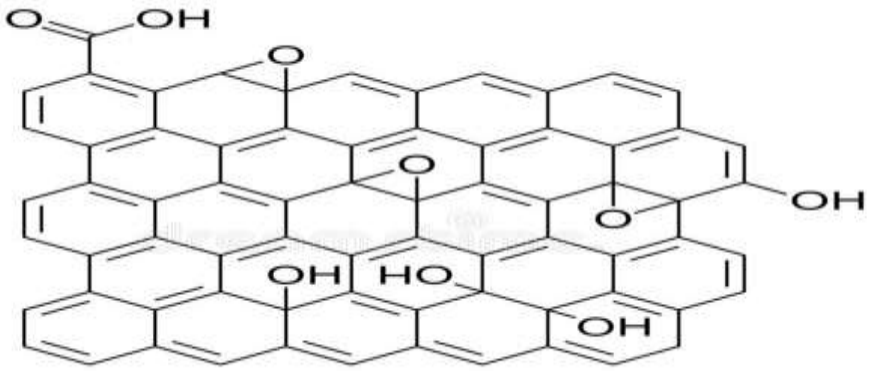

Fig- 2.2: Reduced graphene oxide (rGO).

rGO has several unique properties that make it attractive for various applications.[6] Similar to GO, rGO has a large surface area and high mechanical strength, making it a versatile material for a range of applications.[6] However, rGO also has improved electrical conductivity compared to GO due to the removal of the insulating oxygen-containing functional groups.[6] In drug delivery applications, rGO has been studied as a carrier for various types of drugs, including small molecules, proteins, and nucleic acids. Similar to GO, rGO can protect drugs from degradation and improve their solubility and bioavailability, resulting in enhanced therapeutic efficacy.[7] Moreover, rGO has also been explored for use in energy storage applications, such as in supercapacitors and batteries, due to its high electrical conductivity and large surface area.[7] One of the challenges in using rGO is ensuring its safety and biocompatibility.[7] Although rGO has been shown to be less toxic than GO, concerns remain regarding its potential to induce inflammation and immune response in the body.[7] Therefore, further studies are needed to fully understand the safety and biocompatibility of rGO-based materials.[7] Overall, rGO has shown great potential for various applications, including drug delivery and energy storage.[7] Further research in this area is needed to optimize the design of rGO-based materials and to ensure their safety and efficacy in various applications.[7]

2.3 Graphene quantum dots (GQDs): GQDs are small graphene sheets with a diameter of less than 10 nm.[35] They have unique photoluminescence properties and can be used for bioimaging and drug delivery.[35]

Graphene quantum dots (GQDs) are a type of zero-dimensional graphene-based nanomaterial that have received significant attention in recent years due to their unique properties and potential applications in various fields.[36]

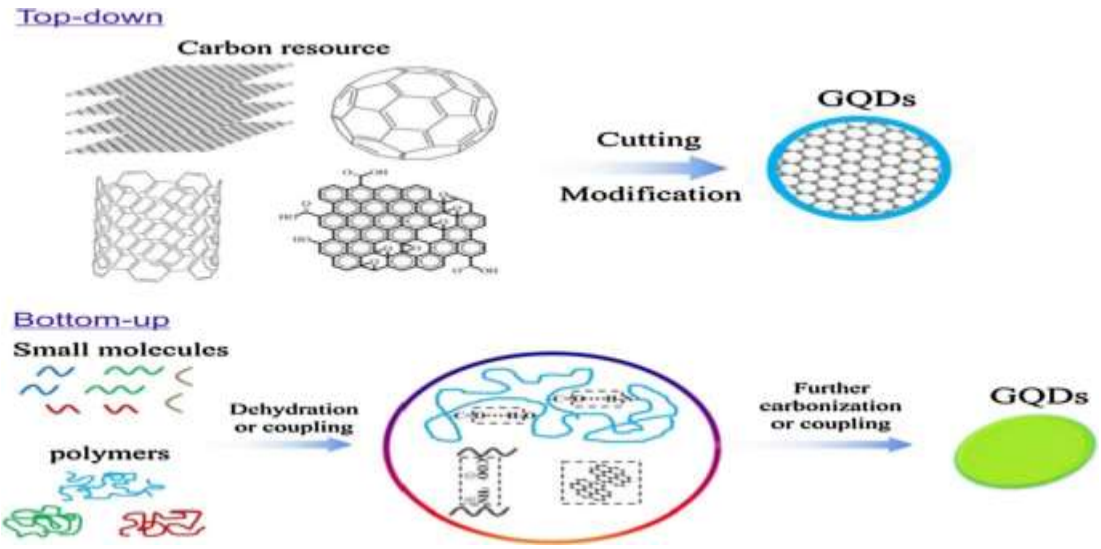

Fig. 2.3: Graphene quantum dots.

GQDs are typically less than 10 nm in diameter and are composed of a few to several layers of grapheme.[36] They exhibit excellent photoluminescence properties, with tunable fluorescence emission that can span the visible to near-infrared regions.[36] This makes them attractive for use in biomedical imaging, sensing, and optoelectronic applications.[36]

GQDs have been studied as a fluorescent probe for bioimaging due to their small size, good biocompatibility, and ability to target specific cells and tissues.[37] They have also been explored for sensing applications, such as for the detection of metal ions, pollutants, and biomolecules.[37] In addition, GQDs have shown promise for energy storage applications, such as in supercapacitors and batteries, due to their high surface area and electrical conductivity[38].One of the advantages of GQDs is their relatively low toxicity compared to other quantum dots, such as cadmium-based quantum dots.[39] However, further research is needed to fully understand their biocompatibility and long-term toxicity.[53] Overall, GQDs represent a promising class of graphene-based nanomaterials with potential applications in various fields, including biomedicine, sensing, and energy storage.[53] Ongoing research is focused on developing new synthesis methods and improving their properties for specific applications.[53]

2.4 Graphene nanoribbons (GNRs): GNRs are narrow strips of graphene with a width of a few nanometers.[42] They have unique electronic and mechanical properties and can be used for drug delivery and bioimaging.[42]

Graphene nanoribbons (GNRs) are strips of graphene with a width of a few nanometers and a length of several micrometers or longe.[42] They can be thought of as an intermediate between graphene sheets and carbon nanotubes.[43] GNRs have attracted considerable attention due to their unique electronic, magnetic, and mechanical properties, which make them promising candidates for a wide range of applications in electronics, photonics, and nanotechnology.[43]

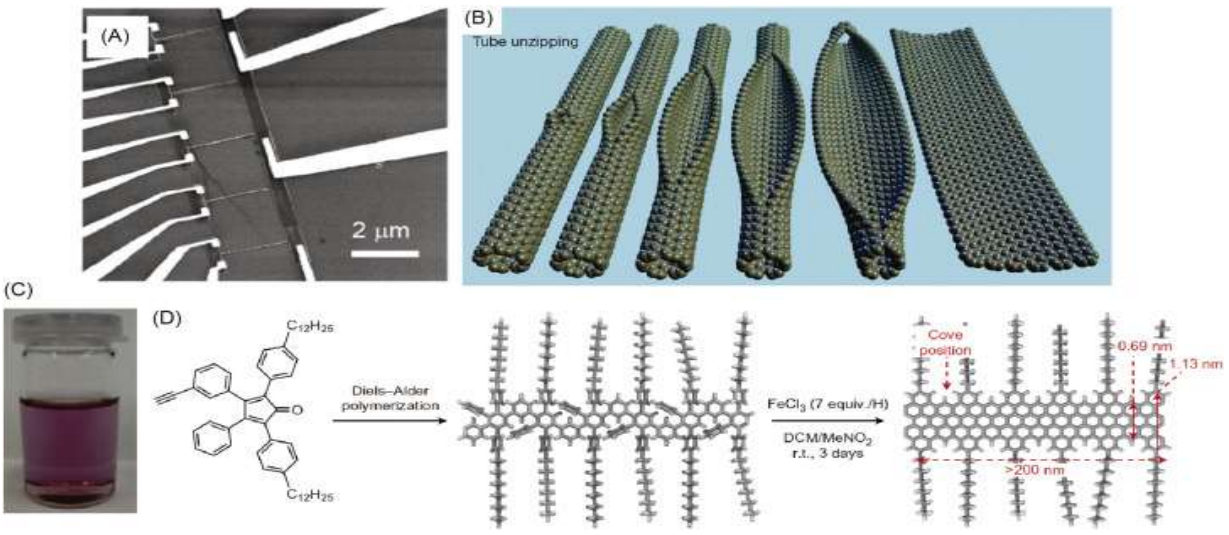

Fig. 2.4: Graphene nanoribbons(GNRs).

GNRs can be synthesized using several methods, including chemical vapor deposition, unzipping of carbon nanotubes, and bottom-up synthesis from molecular precursors.[44] GNRs can have different edge shapes, such as zigzag and armchair, which affect their electronic properties.[44] Zigzag-edged GNRs are predicted to have magnetic properties and can exhibit a spin-polarized current, while armchair-edged GNRs can have semiconducting properties.[44] GNRs have shown potential applications in electronic devices such as field-effect transistors, logic circuits, and sensors.[45] They can also be used as a building block for graphene-based nanomaterials such as graphene quantum dots, nanoribbons-based junctions, and graphene-based nanocomposites.[45] One of the challenges of GNRs is their synthesis, which can be difficult to scale up and control precisely.[45] Additionally, GNRs can be prone to structural defects and edge roughness, which can affect their electronic properties.[45] Researchers are working to develop new synthesis methods and improve the quality of GNRs for practical applications.[46] Overall, GNRs are a promising class of graphene-based nanomaterials with unique properties and potential applications in electronics, photonics, and nanotechnology.[46] Ongoing research is focused on developing new synthesis methods, improving their properties, and exploring new applications.[46]

2.5 Nitrogen-doped graphene (N-graphene): N-graphene has nitrogen atoms substituted for carbon atoms in the graphene lattice.[49] N-graphene has been shown to have improved biocompatibility and can be used for drug delivery.[49] Nitrogen-doped graphene has shown potential as a drug delivery system due to its unique physicochemical properties.[49] Nitrogen atoms can be doped into the graphene lattice, which can modify the electronic and chemical properties of the material.[49] This modification enhances the graphene's ability to adsorb and release drugs.[49]

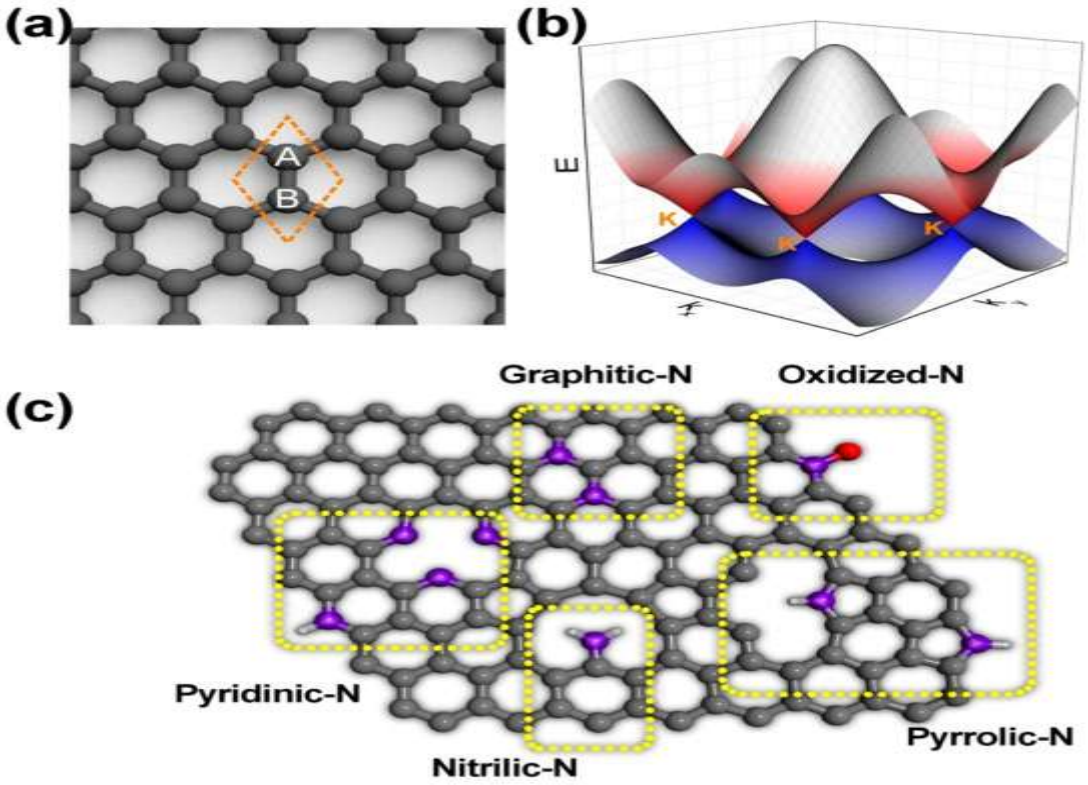

Fig. 2.5: Nitrogen-doped graphene (N-graphene).

In addition, nitrogen-doped graphene can also enhance drug permeability across biological membranes, making it a promising material for drug delivery systems.[52] The high surface area and biocompatibility of graphene also make it an attractive option for drug delivery applications.[52] Several studies have investigated the potential of nitrogen-doped graphene as a drug delivery system for various applications, including cancer treatment, gene therapy, and antimicrobial therapy.[52] However, more research is still needed to fully understand the potential of this material and optimize its properties for specific drug delivery applications.[52]

3. Application

Graphene as a carrier for drug delivery systems have shown great promise in various biomedical applications.[31] Here are some of the applications of graphene as a carrier for drug delivery systems:

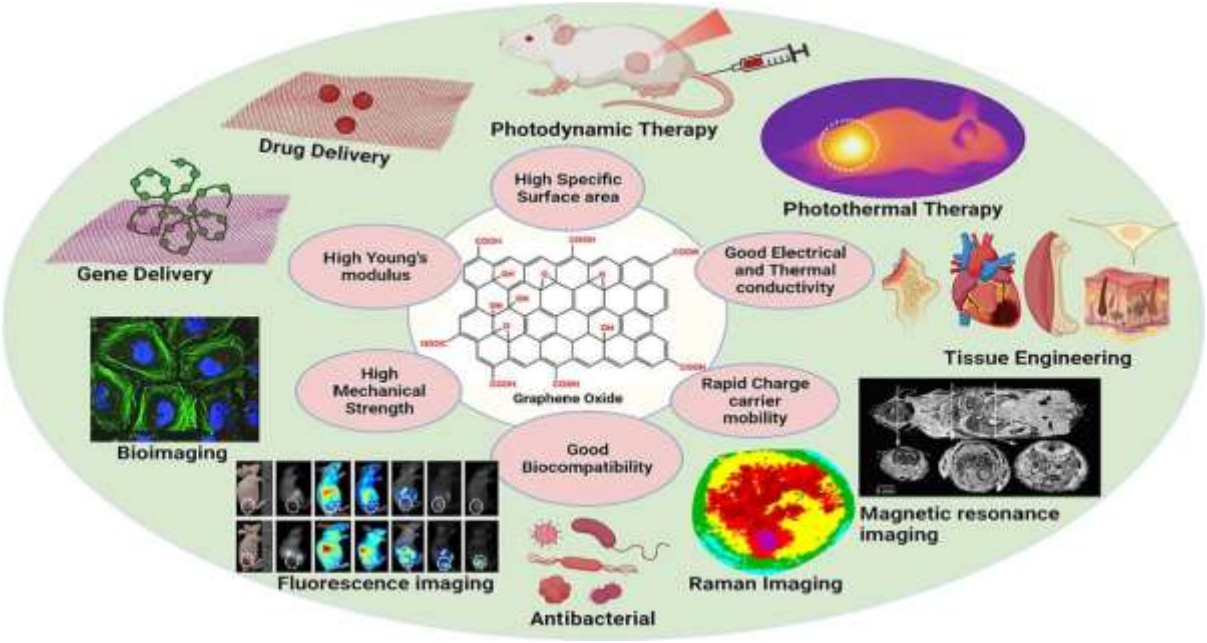

Fig. 3: Various application of grapheme.

3.1 Cancer therapy: graphene as a carrier for drug delivery systems can be used to deliver anticancer drugs to specific tumor sites, improving the therapeutic efficacy and reducing side effects. Additionally, graphene-based systems can be used for photothermal therapy and photodynamic therapy due to their unique optical properties.[28]

3.2 Wound healing: graphene as a carrier for drug delivery systems can be used to deliver growth factors and antimicrobial agents to wounds, promoting tissue regeneration and reducing infection rates.[31]

3.3 Neurological disorders: graphene as a carrier for drug delivery systems can cross the blood-brain barrier and deliver drugs to the brain, making them promising for the treatment of neurological disorders such as Alzheimer's and Parkinson's diseases.[31]

3.4 Drug addiction: graphene as a carrier for drug delivery systems can be used to deliver antagonists and agonists for drug addiction treatment, reducing dependence and withdrawal symptoms.[31]

3.5 Gene therapy: Graphene-based systems can be used to deliver nucleic acids, such as DNA and siRNA, to specific cells, offering potential for gene therapy.[16]

3.6 Tissue engineering: Graphene-based systems can be used as scaffolds for tissue engineering, promoting cell growth, and tissue regeneration.[31]

3.7 Biosensors: Graphene-based sensors can detect biomolecules and be used for diagnostic applications.[16] graphene as a carrier for drug delivery systems have shown potential for targeted drug delivery, bioimaging, and tissue engineering.[30] Their unique properties, such as high surface area, biocompatibility, and low toxicity, make them ideal for drug delivery applications in various biomedical fields.[30] However, more research is needed to optimize these systems for specific applications and address the challenges associated with their use.[30]

4. Challenges of graphene drug delivery

While graphene as a carrier for drug delivery systems have many potential benefits, there are also several challenges associated with their use.[17] Here are some of the main challenges:

4.1 Toxicity: Graphene and its derivatives can cause toxicity to cells and tissues, particularly at high concentrations or when administered for extended periods.[18] Careful optimization of the dosage and surface chemistry of graphene-based systems is required to minimize toxicity.[18]

4.2 Biocompatibility: The biocompatibility of graphene-based systems is a critical factor in determining their clinical usefulness.[19] The surface properties of graphene-based systems can be modified to enhance their biocompatibility, but more research is needed to fully understand the biological responses to these materials.[19]

4.3 Scalability: Large-scale production of graphene-based systems is challenging due to the complexity of the synthesis and the cost of the raw materials. Improving the scalability of graphene-based systems is essential to bring them closer to clinical use.[19]

4.4 Regulatory approval: graphene as a carrier for drug delivery systems are a relatively new technology, and regulatory agencies are still developing guidelines for their use. Obtaining regulatory approval for these systems can be a lengthy and expensive process.[19]

4.5 Stability: Graphene-based systems can be prone to aggregation or degradation, which can affect their stability and efficacy.[19] Careful optimization of the synthesis and storage conditions is required to ensure the stability of these systems.[19]

5. Fabrication methods of graphene based drug delivery systems

There are several methods used to fabricate graphene as a carrier for drug delivery systems, and each has its own

advantages and limitations.[20] Here are some of the most commonly used methods:

5.1 Chemical vapor deposition (CVD): This method involves the synthesis of graphene on a metal substrate by the catalytic decomposition of a hydrocarbon gas.[20] The resulting graphene can be transferred onto a variety of substrates, including biocompatible materials.[21] This method allows for precise control over the thickness and quality of the graphene, making it suitable for drug delivery applications.[21]

5.2 Liquid-phase exfoliation: This method involves the dispersion of graphene flakesin a liquid solvent using sonication or other mechanical methods.[22] The resulting graphene dispersions can be used to prepare drug delivery systems, such as coatings or nanocomposites.[22] This method is relatively simple and scalable, making it attractive for large-scale production.[22]

5.3 Electrochemical synthesis: This method involves the electrochemical reduction of graphene oxide to produce reduced graphene oxide (rGO) or other graphene derivatives.[22] The resulting rGO can be used as a drug delivery platform due to its biocompatibility, electrical conductivity, and surface functionality.[23]

5.4 Bottom-up synthesis: This method involves the assembly of graphene-based materials from molecular precursors.[23] This approach allows for precise control over the structure and composition of the resulting materials, making it useful for drug delivery applications.[23]

5.5 Chemical functionalization: This method involves the modification of the surface chemistry of graphene through the attachment of functional groups or biomolecules.[23] Functionalization can improve the biocompatibility and targeting of graphene as a carrier for drug delivery systems.[23]

6. Future direction of graphene drug delivery system

Graphene as a carrier for drug delivery systems are an exciting and rapidly growing field of research, with many potential future directions.[24] Here are some of the key areas of future development:

6.1 Multifunctionality: graphene as a carrier for drug delivery systems have the potential to serve multiple functions beyond drug delivery, such as imaging, biosensing, and photothermal therapy.[24] Future development in this area could lead to more versatile and effective treatment options.[24]

6.2 Biodegradability and biocompatibility: While graphene is generally considered biocompatible, efforts are underway to improve its biodegradability and further reduce any potential toxicity.[25] Development of biodegradable graphene-based materials could have a significant impact on the field of drug delivery.[25]

6.3 Controlled drug release: The ability to precisely control the release of drugs from graphene-based carriers is a promising area of research. Future developments in this area could lead to more effective and targeted drug delivery, as well as reduced side effects.[25]

6.4 Targeted drug delivery: Targeted drug delivery using graphene-based carriers is already a promising area of research[25] h. Further development in this area could lead to more precise and effective delivery to specific cells or tissues, reducing the potential for side effects and improving therapeutic outcomes.[25]

6.5 Clinical translation: Despite the many promising developments in the field, graphene as a carrier for drug delivery systems have yet to be widely translated into clinical use.[26] Further research and development, including preclinical and clinical trials, will be necessary to bring graphene as a carrier for drug delivery systems into widespread use.[26]

7. Comparison

There are several types of graphene as a carrier for drug delivery systems, each with its own advantages and disadvantages.[27] Here is a comparison of some of the most commonly used graphene as a carrier for drug delivery systems:

7.1 Graphene-based hydrogels: Graphene can be incorporated into hydrogels to create materials with unique properties for drug delivery.[27] These hydrogels can be designed to respond to changes in temperature, pH, or other environmental factors.[27] However, the fabrication of graphene-based hydrogels can be complex, and their mechanical properties may not be ideal for certain applications.[27]

7.2 Liposomes: Liposomes are spherical vesicles composed of a lipid bilayer.[27] They are biocompatible and can encapsulate both hydrophilic and hydrophobic drugs.[27] Compared to graphene as a carrier for drug delivery systems, liposomes have a better safety profile and have been approved for clinical use.[27] However, liposomes have lower drug loading capacity andstability than graphene as a carrier for drug delivery systems.[27]

7.3 Polymeric nanoparticles: Polymeric nanoparticles are made of biocompatible and biodegradable polymers.[28] They have good drug loading capacity and can be engineered to release drugs in a controlled manner.[28] However, they may cause immune responses and have lower mechanical strength than graphene as a carrier for drug delivery systems.[28]

7**.4 Mesoporous silica nanoparticles:** Mesoporous silica nanoparticles have a high surface area and can encapsulate both hydrophilic and hydrophobic drugs.[29] They can be engineered to release drugs in a controlled manner and have good stability.[29] However, they may cause toxicity and inflammation in vivo.[29] Compared to these drug delivery systems, graphene as a carrier for drug delivery systems have several advantages, including high drug loading capacity, excellent mechanical strength, and the ability to penetrate biological barriers.[29] However, they also face challenges such as biocompatibility, scalability, and regulatory hurdles.[29]

8. Regulatory and ethical considerations of graphene as a carrier for drug delivery systems

Safety regulations, clinical trials, and social implications. As with any new drug delivery system, graphene as a carrier for drug delivery systems must undergo rigorous safety and efficacy testing before they can be approved

for use in humans.[30] Regulatory bodies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have established guidelines for the development and approval of drug delivery systems, including nano carriers such as graphene-based systems.[30] Some of the key safety regulations for graphene as a carrier for drug delivery systems include testing for biocompatibility, toxicity, and potential environmental impact. In addition, clinical trials must be conducted to determine the safety and efficacy of the system in humans.[30] These trials must follow ethical guidelines and ensure that patients are fully informed about the potential risks and benefits of participating.[30] In terms of clinical trials, graphene as a carrier for drug delivery systems are still in the early stages of development.[31] More research is needed to fully understand their safety and efficacy, as well as any potential long-term effects.[31]

There are also social and ethical implications to consider with the use of graphene as a carrier for drug delivery systems.[31] For example, there may be concerns about the environmental impact of producing and disposing of graphene-based materials.[32] In addition, there may be questions about access to these new technologies and the potential for unequal distribution of benefit[32] ts. Overall, the development and use of graphane-based drug delivery systems must be guided by careful consideration of safety and efficacy, as well as ethical and social implications. Continued research and dialogue between scientists, regulators, and the public will be essential to ensure that these systems are developed and used in a responsible and beneficial manner.[32]

9. Drug loading methods for graphene based drug deliverysystem

Drug loading methods for graphene as a carrier for drug delivery systems typically involve physical or chemical methods to attach or encapsulate the drug molecules onto or within the graphene surface.[33] Here are some common drug loading methods:

9.1 Non-covalent adsorption: This involves simply adsorbing the drug molecules onto the surface of the graphene through weak van der Waals interactions or π-π stacking interactions.[33] This method is simple, fast and has a high loading capacity but the drug may be released easily.[33]

9.2 Covalent functionalization: This method involves attaching functional groups to the graphene surface that can covalently bind with drug molecules.[34] This method offers a strong and stable bond but may require additional steps for preparation and purification.[34]

9.3 Encapsulation: This involves encapsulating the drug molecules within the graphene, typically by forming a layer of graphene around the drug molecules.[35] This method offers protection for the drug from degradation and release but may require additional steps for preparation.[35]

9.4 Electrostatic interaction: This involves electrostatically binding the drug molecules onto the graphene surface by forming an ionic complex.[36] This method is simple and fast but may have limited drug loading capacity and stability.[36]

The choice of drug loading method will depend on several factors such as the desired drug release profile, the type of drug molecule, the stability and solubility of the drug, and the intended application.[37] It is important to optimize the drug loading method to achieve the desired drug delivery efficiency and minimize potential toxicity.[38]

10. CONCLUSION

In conclusion, graphene as a carrier for drug delivery systems have emerged as a promising platform for enhancing drug efficacy and specificity, while reducing toxicity. The unique physical, chemical, and biological properties of graphene make it an ideal carrier for delivering therapeutic agents to targeted tissues. However, there are still several challenges that need to be addressed before these systems can be translated to clinical use.

The biocompatibility of graphene needs to be carefully evaluated to ensure its safety for human use. Large-scale production of graphene at a reasonable cost is also a challenge that needs to be overcome. In addition, reproducible synthesis methods are required to ensure consistent quality of graphene as a carrier for drug delivery systems. Despite these challenges, graphene as a carrier for drug delivery systems have shown significant potential in preclinical studies, demonstrating improved pharmacokinetics, bioavailability, and targeted delivery compared to conventional drug delivery systems. Further research is needed to optimize the production and biocompatibility of graphene and to develop effective graphene as a carrier for drug delivery systems for clinical translation. Overall, the use of graphene as a drug carrier represents an exciting avenue of research that could lead to significant advancements in drug delivery and therapeutic outcomes.

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