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A Brief Review on the Synthesis, Cytotoxixity, Bioavailability and Various Applications of Graphene Nanomaterials

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Abstract **Review Article**

The physicochemical characteristics of graphene-based nanometrics are ideal for a variety of electronic, telecommunication, energy, and healthcare applications. Human and environmental exposure to graphenic nanomaterials increases due to the synthesis, characterization and mass processing of graphene as well as the growth of biomedical and consumer products based on graphene. Throughout this paper, we analyze the various available synthetic methods of graphic nanomaterials and discuss in-vitro and in-vivo mammalian cell-associated biological structure and toxicity of these nanomaterials. Different synthesis strategies were developed to generate the chemical and physical properties of graphene nanometries. As such their relationships with cells and organs also change. Literature published bio-structure and cytotoxicity results from graphene nanomaterials. In particular, graphene nanomaterials in in-vitro cell cultivation and animal models may contain toxic chemical residues, interfere with graphene cell interactions and complicate interpretation of the experimental results. Synthesis methods including exfoliation of the liquid phase and wet chemical oxidation require harmful organic solvents, surfactants, strong acids and oxidants to dissolve graphite flakes. Such biological and inorganic molecules, which interfere with living cells and tissues, activate toxins or eventually cause necrobiosis, can be deposited with the final graphene products. Residual chemicals in living cells pose a high risk of toxicity from graphene. This study summarizes the synthesis of nanomaterials, cytotoxicity, bioavailability, and various applications.

Keywords: Grapheme, Synthesis, Cell culture, Biocompatibility, Toxicity.

INTRODUCTION

The carbon allotrops are graphite, diamond, carbon nanotube (CNT) and complementary. The most common allotropic graphite is madeup of hexagonally packed sp2 hybridized carbon sheets, stacked at a distance of 0.34 nm from the weak forces of Vander Waals. A graphene is the single graphite layer packed in a wave-filled crystal grid with one atomic-scale thickness. Boehm, Setton, and Stumpp coined the word graphene in 1994 [1].

In 2004, the University of Manchester research group Novoselov and Geim successfully exfoliated a single graphite layer using simple scotch tape methods. This single-level graph shows excellent intrinsic properties which led to the “Nobel Prize” for Physics in 2010 for Novoselov and Geim. Graphene is also a versatile building block for other carbohydrating structures, such as 0D compleerene, 1D carbon nanotube and 3D graphite, respectively. The two-dimensional graph has special physicochemical features [2-6]:

Graphene has become a multi-functional material for a broad variety of applications including sensors, solar cells, fuel panels, photocatalytics, supercapacitors, and batteries [7-11].

Nanotechnology is a multidisciplinary field of study covering a range of fields including biology, chemistry, electronics, materials, physics and medical sciences. Nanotechnology involves the design and production of new materials and devices by manipulating nanometer-scale material properties and functions. The biological, mechanical, physical and chemical behavior of these materials varies significantly from their bulk counterparts. Nanotechnology is very exciting to create and synthesize nanomaterials with different biological, physical, chemical and mechanical properties. Through the application of nanotechnology in the medical sector, scientists can create effective new materials and technologies for the exposure and obstacle of malignant diseases, advanced implants and highly bio-compatible artificial protheses. Carbon materials, such as carbon nanotubes and maps, have an outstanding module and mechanical efficiency, a high light transmission and excellent electrical conductivity [12]. This was supported by the use of this material for electrical apparatus, construction products, medical supplies, medical implants, etc. [13, 14]. For example, because of their hollow structure one dimensional (1D) carbon nanotubes (CNTs) promise drugs in biological cells. CNTs with needlelike features can penetrate easily into the plasma membrane and thus bear therapeutic molecules effectively. Cells penetrating nanotubes can, however, also damage organic cells because they cause significant toxicity and apoptosis [15]. Electron microscopic studies have revealed that nanotubes exist in cytoplasms, resulting in oxidative stress, reduced metabolic activity and subsequent cell death [17]. In this respect, the bio-distribution, the size, and shape of carbon nanotubes impede the application in the clinical area. This consists of simple building blocks, including GQD and 0d bucky ball, 3D graphite, and 1D carbon nanotube for all other dimensional carbohydrates [18].

Graphene was first isolated by “Geim and Novoselov” through mechanical cleavage using a scotch tape to fix the flakes of graphite layers. Mechanically exfoliated, defect-free and pure graph surface, but very low in size. This application is limited mainly to work on the mechanical and optical properties of pure graphene. Researchers therefore performed several studies to synthesize graphic oxide (GO), reduced graphic oxide (RGO), and heat-reduced graphic oxide (TRG) to a wide degree. In the telecommunications, telecommunications and aeronautical industries, the outstanding electrical, mechanical and optical characteristics of the graphema sheets and of GQDs make this attractive [19-21].

Graphene, their derivative, and GQDs have provided promising materials for biomedical use such as tissue engineering, biosensors, bioimagery, pharmaceuticals, and photothermal therapy. GQDs are typically photoluminescent due to a quantum containing effect. The presence of GQDs (< 2 mg/mL) that leads to the healthy development of zebras. When using graphene-based materials for biomedical applications, biocompatibility is a significant concern. Graphene and its derivatives are frequently inconsistent in their biocompatibility with literary works [22].

Chang *et al*., find that A549 (human basal epithelial basal cells) is not GO's and has no apparent cytotoxicity. However, GO appears to cause oxidative stress depending on the dose in cells, which decreases the cell viability to a high standard. Dose and size are related to these effects. Wang *et al*. GO also show dose-dependent toxicity to human fibroblast cells and mice. Tests showed that GOs of less than 20 g/mL have no toxicity to human fibroblast cells. Natural cytotoxicity is observed at doses higher than 50g / mL, including reduced cell adhesive and cell apoptosis. Small dose (0.1 mg) and intermediate dose (0.25 mg) GO in vivo mice experiments do not indicate any acute toxicity, but chronic toxicity is caused by a high-dose (0.4 mg). Yang *et al.*, researched in-vivo polyethylene glycol (PEG)-functional graphene biodistribution in mice. We have shown that PEGylated graphene is not significantly toxic in doses of 20 mg/kg for three months [23-28].

THE STRUCTURE OF GRAPHENE

Basics Structure

Carbon is the sixth element in the Periodic Table with an electronic configuration of 1s22s22x22Py 12Py 12Pz0. 2pz electron-free energy is kept for ease, even though it is equal to 2px and 2py. Six electrons, four of which are electrons of interest, surround the nuclear carbon nucleus. These electrons are capable of forming three forms of carbon-valence hybridization: sp, sp2, and sp3. Since carbon atoms share S2 electrons with their three carbon atoms, they form a planar wave structure, also called monolayer lines. During the typical sp2 hybridisation, the μ off-flane bond consists of 2pz orbital layers perpendicular to the planar structure of two adjacent carbon atoms. In contrast, the in-plane μ bond consists of the hybridized sp2 orbitals (2s,2px,2py). The resulting covalent, interatomically short bond, about 1.42Å, which makes the bond even more potent than the hybridized carbon sp3 – carbon bonds in diamonds with an extensive mechanic function of monolayers, including a Young's 1 TPa module and a 130.5 GPa tensile strength. With a semi filled α-band, the steering band and valence band with a zero-band distance allow free moving electrons to be produced in the monolayer graph. In the μ-bonds, the interaction between adjacent two-layer graphs and multi-layer graphs is also mild.

Synthesis of Graphene-Based Nanomaterials

Graphene can typically be synthesized up and down from both directions. The top-down route includes liquid exfoliation, micromechanical graphite cuttings, and the exfoliation of metallic graphite, accompanied by chemical or thermal RGO or TRG processes. The processing path from the bottom up involves the deposition of chemical vapor and SiC substratum epitaxial growth [29].

Epitaxial Graphene on SiC Wafers

Graphene films on SiC wafers can form at temperatures (usually more than 1000 C) by sublimating Si atoms from high vacuum wafers (UHV). As a result, graphene is left to the surface of the wafer. Nevertheless, small size SiC wafers, the high cost, and the need for UHV high-temperature equipment preclude this method from being used in commercial large-scale graphic production [30, 31].

Chemical Vapor Deposited Graphene Films

A chemical vapor-deposit is usually used to produce great monocle graph films on transition metals (Fe, Ni, Co, Pt, Ru) by allowing a high-temperature film reaction chamber such as methane, ethane, or propane to be hydrated. Cu or Ni substrates are common because of their low cost for the decomposition of hydrocarbon gasses. Then the thin films are transferred to different substrates like SiO_2/Si, glass, or flexible polymer (PET). The graphics are processed in two steps and extended. The first step is the first carbon pyrolysis precursor. The development of dissociated carbon atoms follows the graphical structure creation. CVD graphene growth is typically achieved by a surface adsorption cycle in a Cu substratum with a low carbon solubility. The precursor of carbon breaks down and only adsorbs the metal surface, followed by migration and growth. Graphene on Ni is made from carbon segregation and precipitation, on the other hand. Carbon species are broken down and distributed over a high carbon metal surface at high temperatures to create a robust solution. The cooling increases carbon solubility and allows carbon atoms to move from the metal and graph on the Ni surface. Graphene foil growth and consistency can be affected by various factors, including material types and CVD parameters such as gas content of the precursor, concentration, flow rate, and temperature are measured. The graphene films of random graphene islands are high grain density polycrystalline. Such grain limits significantly degrade the electrical characteristics of graphic films as they serve as the electron dispersion core and reduce the mobility anticipated. Graphic films with small grains or even single crystal graphic films with lower grain borders must be created in this regard. In the past, Xu *et al*., developed single-crystal graphene (5, 50 cm^2), on the copper surface of the graphene islands, in a single meter Cu (111) foil and epitaxially. The as-synthesized graphemetric film had up to 23,000 $cm^2\ V^{-1}\ s^{-1}$ mobility at 4 K. For the development of bendable screens, displays and optoelectronic products, high graphic CVD-grown films are utilized [32-36].

Liquid Phase Exfoliation

Its low cost and simplicity make it a scalable route for mass graphene production. Graphite is dispersed between graph interlayers in a solvent in the absence or presence of surfactants. Ultrasound or shaving can promote graphite exfoliation in graph sheets. A purification step is taken to generate single, multi-faceted graph sheets. This technique allows exfoliated graph sheets to synthesize solvent suspension. Since graphene flakes' exfoliation and stability in the specific medium is dependent on organic solvents, surfactants, and strong acids, they can cause environmental pollution problems. Graphene sheets also have difficulty removing residual surfactants. Many organic solvents (*e.g.*, N-methyl 2-pyrrolidone (NMP); N, N-dimethyl-formamide (DMF); dichlorobenzene (DCB) are highly toxic; cell toxicity induction may be possible, and cell manipulation should be avoided.

Chemical and Thermal Reduction of GO'

Graphene oxide is a derivative of graphene which is formed by the chemical oxidation of solid oxidants by graphite flocks. Using sulphuric acid, sodium nitrate, and potassium permanganate mixtures in a strong stirring or sounding cycle, Modified Hummers is used to produce GO. Suspension is saturated with water, and then added hydrogen peroxide to increase oxidation, followed by water rinse. The disadvantages are extended processing times and toxic gas output (NO_2 and N_2O_4). Tour and colleagues adapted this method to address these problems by replacing sodium nitrate with phosphoric acid in mixed H_2SO_4 / H_3PO_4 ratio (9:1). This method's advantage is reducing toxic gas formation. The drawbacks include substantial $KMnO_4$, boring sampling, filtration, centrifugation, and washing. Thus, several techniques were introduced to further alter the Hummers process, such as using K2FeO4 as a effective oxidizing agent instead of $KMnO_4$ and eliminating $NaNO_3$ in GO preparation.

Nanocomposites Graphene-Polymer

Pure graphene has an exceptionally high elastic module of about 1 TPa and a resistance of 130 GPa, excellent optical clearance of 97.7% and a good electric conductivity and mobility of 2,105 $cm^2\ V^{-1}\ s^{-1}$. Graphene is an appealing filler material for nanocomposites 40 polymers. Through adding micro- or nanoscales fillers, the output of high-flexibility polymers can be optimized for various applications. Polymer composites inherit beneficial properties of their components and, in addition, polymers guard against mechanical damage to embedded fillers [37-41]. Because of their light weight, ease of manufacture and low costs, the conventional polymer composites are widely used in the biomedical and industrial sectors as structural components. Nonetheless, the desired biological, mechanical and physical behavior includes high-volume filler material (30%). The properties of the polymer microcomposites are affected by large volume filler material. Graphene-based nanomaterials can be used at low loading loads to fill and reinforce polymers [42-47].

The GO element is still substantially higher than biopolymers, including polylactic acid (PLA) of about 2.7–3 GPa and 0.4 GPa (PCL). GO can be used to increase the mechanical performance, thermal stability, and biocompatibility of nanocomposites of GO / PLA and GO / PCL. The biocomposite polymer can be made in different ways, including mixing, melting, and electrospinning of solutions [48-50].

CONCLUSION

This study summarizes the synthesis, cytotoxicity, bioavailability and specific applications of nanomaterials. Graphene toxicity has been shown to rely on scale, shape, cleanness, post-processing stages, oxidation state, dispersion, functional groups, route and dose, and exposure time methods. Both studies raise the understanding of synthesis, cytotoxicity, biological health services adaptability and increased risks to human health. This approach opens new possibilities for biomedical applications in orthopedics for the development of advanced bone stabilizers, fabrics and implants. More safety should be tested and examined before clinical use to make sure that these polymer nanocomposites are biocompatible with human tissue.

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