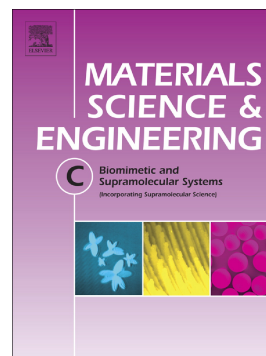


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Advancements of graphene-based nanomaterials in biomedicine

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ABSTRACT Graphene-based nanomaterials, such as graphene oxide and reduced graphene oxide, have been attracting increasing attention in the field of biology and biomedicine over the past few years. Incorporation of these novel materials with drug, gene, photosensitizer and other cargos to construct novel delivery systems has witnessed rapid advance on the basis of their large surface area, distinct surface properties, excellent biocompatibility and pH sensitivity. Moreover, the inherent photothermal effect of these appealing materials enables them with the ability of killing targeting cells via a physical mechanism. Recently, more attentions have been attached to tissue engineering, including bone, neural, cardiac, cartilage, musculoskeletal, and skin/adipose tissue engineering, due to the outstanding mechanical strength, stiffness, electrical conductivity, various two-dimensional (2D) and three-dimensional (3D) morphologies of graphene-based nanomaterials. Herein, emerging applications of these nanomaterials in bio-imaging, drug/gene delivery, phototherapy, multimodality therapy and tissue engineering were comprehensively reviewed. Inevitably, the burgeon of this kind of novel materials leads to the endeavor to consider their safety so that this issue has been deeply discussed and summarized in our review. We hope that this review could offer an overall understanding of these nanomaterials for later in-depth investigations.

KEYWORDS: *graphene; physicochemical properties; biocompatibility; bio-imaging; delivery; phototherapy; tissue engineering*

1. Introduction

Carbon is one of the essential elements on the earth. Nanocarbon opened a door to these novel nano-sized carbon allotropes, which basically contain three different dimensions, zero dimension (0D), one dimension (1D) and two dimension (2D). This is represented by fullerene, carbon nanotube, graphene respectively (Fig 1a,b,c). The crazy chasing for carbon nanomaterials began with the first discovery of the 0D fullerene (C₆₀) in 1985 by Kroto et al.^[1] Following that, Iijima brought 1D carbon nanotubes (CNTs) into the awareness of the scientific community in 1991.^[2] In 2004, Andre Geim and Nosovlov successfully isolated single-layer graphene from graphite by mechanically cleaving a graphite crystal, pushing this kind of nanomaterials development to an exciting climax once again.^[3] Their studies have confirmed that graphene exists in a 2D honeycomb-type lattice structure formed by a single sheet of sp²-bonded carbon atom. It is a milestone that firstly provided solid evidence to support the long existing graphene theory which can be traced back to the year of 1947.^[4]

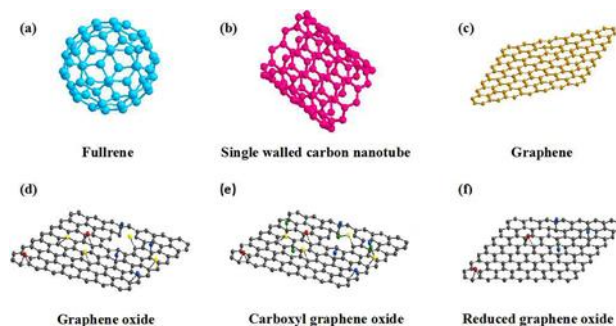


Figure 1. The structure of fullerene (a), single walled carbon nanotube (b), graphene (c), graphene oxide (d), carboxyl graphene oxide (e) and reduced graphene oxide (f).

Since then, the potential applications of graphene-based nanomaterials in biomedical field have been intensively explored for the unique physicochemical properties associated with these materials. Specially, the progress has been made towards drug/gene delivery,[5, 6] phototherapy,[7, 8] cellular growth and differentiation,[9, 10] biosensors,[11-13] bio-imaging,[14,

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