Nanocomposites from Polyethylene Glycol Modified Graphene and Transferrin as Highly Targeted Antitumor Drug Carriers

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Abstract

We present our recent efforts on synthesis of nanocomposites from polyethylene glycol (PEG) modified graphene incorporated with Transferring (Tf) and their application in drug delivery. Pegylated graphene (PG) was prepared using a facile but efficient technique: the edge-functionalized ball milling (EFBM) method. PEG will edge-functionalized the graphite layers during the initial step of ball milling. Exfoliation of graphene nanosheets can be realized by expanding the layered spaces with increasing PEG chains and ball milling shear forces. The resulting PG provides additional advantages for drug delivery including unique size and huge surface areas arising from graphene, and excellent biocompatibility, hydrophilicity and pH sensitivity with the addition of PEG. Tf was further introduced into the PG via a facile amidation process to enhance targeted ability of the resulting nanocarriers. Anticancer drug e.g. doxorubicin (DOX) was subsequently encapsulated in the PEG-Tf for suppression of tumor cells such as the typical choroidal melanoma cell line: OCM-1 cell. Atomic forace microscopy confirmed that the thickness of the as-synthesized PG was around 1.3 nm. DO loading ratio at the PG and PG-Tf were found to be 58% and 50% respectively, much higher than the general drug delivery system. The targeting and suppression ability of PG-Tf-DOX towards OCM-1 cells were determined by the Transwell co-culture technique and the CCK-8 assay respectively. Much lower cell viability of OCM-1 cells than that of ARPE-19 cells was obtained when cells were co-cultured with PG-Tf-DOX, confirming the superb targeting ability of PEG-Tf-DOX towards OCM-1 cells. A 3D cell culture model was further used to simulate the antitumor effects. The changed volumes of simulating solid tumor demonstrated that PG-Tf-DOX had a excellent antitumor effect. Release of DOX from the PG-Tf exhibited a highly pH-sensitivity. Much faster release in acidic solution (tumor environment) was observed, suggesting great possibility of the controlled release of DOX from the PG-Tf-DOX at the tumor environment.