HYBRID NANOPARTICLES FOR BETTER MEDICINE

NANOPARTICULES HYBRIDES POUR UN MEILLEUR MEDICINE

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Nanoparticles (NP), having no or less cytotoxicity with improved stability in water-based suspensions and versatile surface functions is one of the major direction in development of novel candidate for nano-biotechnological and medical applications as imaging probes, materials for cancer therapy and as drug carriers. Here we present our latest achievements in designing, preparation investigation and application of hybrid 1) carbon-based materials and particularly a) nanodiamond particles (NDs), and b) graphene derivatives (GO) 2) silicon-based materials and particularly nanoparticles of a) silicon carbide (nSiC) and b) silicon (nSi), and 3) hybrid core-shell nanosized material with functional core: a) magnetic, b) metallic (Au nanorods) protected with biocompatible shell. We report elaborated strategy and methodology for preparation and functionalization of biocompatible nanoparticles in order to apply them in: a) photothermal cancer therapy and b) triggered drug delivery and release for better medicine.

Major problem in biomedical application of nanodiamonds is their small surface area and difficulties in surface modification. We developed a simple strategy for simultaneous immobilization of targeting molecules, drugs and imaging agents on the NDs nanostructure for the convenience of detection and targeted treatment. To validate the concept, a model material carrying triethylene glycol and azide modified dopamine anchors (dop−EG and dop−N3) was fabricated. The presence of EG functionalities rendered NDs soluble in water and biological media, while the −N3 group allowed post-synthetic modification of the NDs using "click" chemistry. The concept was used to develop multifunctional NDs. We demonstrated that NDs with immobilized carbohydrates have specific interaction with bacterial membrane proteins. Such specific interaction was used for develop new bioanalytical tools. It was also discovered that NDs with immobilized carbohydrates strongly inhibit of both E. coli and Staphylococcus aureus adhesions. Mannan-modified NDs show strong interactions with uropathogenic E. coli., suggesting the effectiveness of photochemically formed glyco-NDs for disruption of E. coli-mediated biofilms. Alternatively, photochemical linking of unmodified mono-, di-, and polysaccharides to nanodiamond particles pre-modified with perfluorophenylazide ligands is a general method for coupling underivatized carbohydrates to diamond nanostructures. The resulting glyco-NDs maintained their expected binding affinity and specificity towards their partner lectins.

One of the focal subjects in insulin delivery is the development of insulin formulations that protect the native insulin from degradation under acidic pH in the stomach. We demonstrated that a graphene oxide (GO) based matrix can ensure the stability of insulin at low pH. The insulin-containing GO matrices were stable at acidic pH, while insulin was released when exposed to basic solutions (pH = 9.2). Using Xenopus laevis oocytes as a model we showed that the meiotic resumption rate of GO and GO–MPdop remained unaltered when pre-treated in acidic conditions. These results suggest that GO based nanomatrices are promising systems for treatment of patients with insulin deficiency. One of the major limitations of reduced graphene oxide (rGO) application is its low stability of water suspensions. It was demonstrated that the integration of rGO with PEG drastically increase the rGO solubility under physiological conditions - no aggregation observed even after 6 months of storage. This research opened the gate for application of rGO in biosensors and nanobiotechnology. For example, unique properties of rGO were revealed in its bioanalytical application for detection of important mutagen - peroxynitrite. We discovered also that such stabilized rGO nanosheets can be decorated with metals (Au, AuPd) nanoparticles that essentially increased their efficiency in plasmonic photothermal cancer therapy.