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Ultrasound responsive proapoptotic drug delivery platform for image-guided therapeutics

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Recently, liposomes-microbubble conjugates have emerged as a promising ultrasound (US)-responsive platform for cancer therapeutics. However, these are limited by their size in terms of tumor penetration. Additionally, there have been no attempts to enhance the smartness of the liposomes-bubble conjugates which have been used only as passive carriers. The present study explores submicron sized (756±180.0 nm), US-responsive, PhosphatidylSerine (PS)-based Paclitaxel-Liposomes-nanoBubble Conjugates (PSPLBC) with an additional pro-apoptotic effect towards enhanced anti-cancer efficacy and image-guidance. The developed PSPLBC underwent cavitation in response to US trigger, exhibiting in vitro pulsatile release with a 10-fold increase in cellular internalization as compared to control. The PS-containing formulations were found to be pro-apoptotic and exhibited strong synergism between PS and paclitaxel (Combination Index, CI < 0.1). This resulted in significantly high anti-tumor efficacy both in vitro and in vivo conditions (98.3±0.8% tumor growth inhibition, TGI) and 100% survival rate as compared to placebo control. Significant reduction in tumor proliferation index and microvessel density (MVD), as well as significant increase in apoptosis, were observed for the treated tumor sections. Further, the intravenous (IV) administration of PSPLBC enhanced the tumor US-contrast by 2-fold as compared to SonoVue®, a commercial ultrasound contrast agent (UCA), suggesting the image-guided therapeutic potential of the developed pro-apoptotic liposome-nanobubble conjugates.

These results show the potential of the developed liposome-nanobubble conjugate as a sub-micron-sized, smart pro-apoptotic platform for US-image-guided and triggered delivery of a variety of drugs in case of various biomedical applications such as cancer.

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Toward unified model of graphene growth on transient metals of high and low carbon solubility in CVD processes: Comparison of theory with experiments for Ni and Cu foils

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Outstanding physical, chemical, optical, mechanical and electronic properties of graphene are very promising for applications in novel nanocomposite materials and nanoelectronic devices. Recently chemical vapor deposition has emerged as the most efficient, scalable and cost-effective method of graphene synthesis. This work is aimed at generalization of results of our previous studies on nanomaterials synthesis in CVD processes. It is shown that isothermal graphene growth on Cu and Ni foils can be described by similar mathematical formulation that includes processes of chemisorption and catalytic decomposition of hydrocarbon molecules on metal surface, diffusion of C atoms in transient metal catalyst, its nucleation and extrusion in the form of graphene. The Ni and Cu foils were chosen as limiting cases and as the most commonly used transient metal catalysts with high and low carbon solubility respectively. The major difference is in spatial distributions of carbon diffusive fluxes: in the bulk of metal for nickel and in radial direction toward nucleation centers in thin molten surface layer for Cu. Dependencies of domain growth velocity and graphene growth time on hydrocarbons concentration and process temperature are calculated. Calculated results for Ni and Cu foils are compared with each other and verified using data from in situ graphene growth experiments. Effect of domain morphology on graphene growth characteristics is studied numerically. Time dependences of surface areas, in radiuses, circumradiuses and growth rates of graphene domains in the form of regular polygons are analyzed in detail as functions of the number of angles in polygons. Calculations reveal that triangular graphene domains grow twice as fast as hexagonal domains for comparable CVD conditions. It is shown that the decrease of the process temperature and/or increase in hydrocarbon concentration results in more prominent dependency of dynamical characteristics of graphene domains growth on its geometrical form. The distinct feature of this work is a new generalized framework that permits to describe dynamics of graphene growth with domains of different morphology on high as well as low carbon solubility transitional metal catalysts. Obtained results can be applied for the rational design of catalytic CVD processes for synthesis of graphene domains with properties customized to specific applications (e.g. hybrid nanocomposites) and compatible with its direct integration into micro- and nanoelectronic devices.

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