Effect of chemically modified nanodiamonds on 3D human atherosclerotic plaques model

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Atherosclerosis is the major underlying cause of cerebrovascular and cardiovascular diseases [1]. It is considered that this disease is linked to hypercholesterolemia and the accumulation of inflammatory cells in the artery wall. Inflammation is involved in the atherosclerotic process by recruiting leucocytes, promoting plaque growth, and inducing plaque destabilization. Formation of the plaque usually continues over decades, starting with early lesions formation, which may occur in early adolescence. The disease progression depends on many factors, such as gender, genetics and some well recognized risk factors- obesity, diabetes, hypertension, smoking, aging, etc. [2]. The development of advanced atherosclerosis is a slow progressive process that starts in childhood and remains asymptomatic for many decades, with complications such as myocardial infarction, stroke, or peripheral ischemia usually occurring in later life [3]. In the last decades, stenting became an effective minimally invasive therapy for reducing coronary artery blockage and achieved great success. However, in-stent restenosis is still a clinical problem, and no effective treatment for removing atherosclerosis plaque in human vessels exists.

This study aimed to develop a new generation of unique cardiovascular stents through the innovative double-layer coating. A hybrid biodegradable nanocomposite sub-coating layer serving for anti-plaque effect with a chemical functionalized Fe@C or nanodiamonds (NDs) containing lipophilic organic groups to promote the reverse cholesterol transport.

NDs have been proposed for various biomedical applications, including bioimaging, biosensing, and drug delivery, owing to their physical-chemical properties and biocompatibility. Different surface functionalization methods have been developed, varying the ND's surface properties and rendering the possibility to attach biomolecules to interact with biological targets. The NDs used in this study were functionalized in three steps, shown in Figure 1. Following the physical-chemical characterization of arylated NDs, their cytotoxicity was analyzed in vitro as a significant concern for future clinical translation. This study used rapid, sensitive, and reproducible 2D and 3D models for nanotoxicity tests. We optimize the conditions for using the 3D atherosclerotic plaque model and analyze the toxicity in the presence of NDs. NDs were observed by laser confocal fluorescence microscopy and fluorescence lifetime imaging. Using the 3D human atherosclerotic plaque model for a safety evaluation and treatments with NDs-based nanolabel will be discussed.

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References

[1] Soufi M., Sattler A.M., Maisch B., Schaefer J.R. Herz 27 (2002) 637-648.
[2] Biros E., Karan M., Golledge J. Curr. Genomics 9 (2008) 29-42.
[3] Blanco-Colio L.M., Martin-Ventura J.L., Vivanco F., Michel J.B., Meilhac O., Egido J. Cardiovasc. Res. 72 (2006) 18-29.

Figures

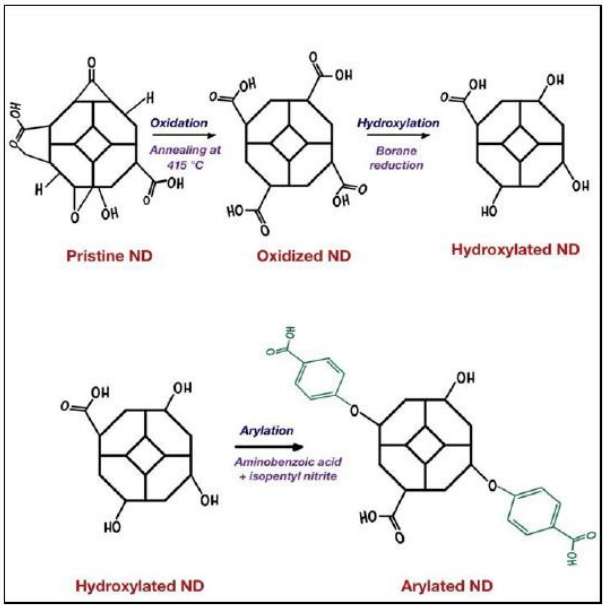

Figure 1. NDs surface functionalization steps. 1 - The NDs oxidation by thermal annealing at 415 °C, 2 - Hydroxylation by using borane reduction treatment, 3 - Arylation by addition of aminobenzoic acid and isopentyl nitrite.