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LETTER

Nanostructured Materials as an Analytical Strategy to Unravel and Treat Human Diseases: The Practical Challenges Behind the Theory

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In recent years, the world has witnessed important progress in the field of nanotechnology, which has strongly impacted the various fields of science and industry, creating new applications in electronics,[1] medicine,[2] and energy storage.[3] In this sense, several nanoscale materials with different compositions have been produced and reported in the literature.

Nanomaterials can be classified according to their composition. For example, silicon dioxide (SiO_2),[4] quantum dots (QDs),[5] carbon dots (CDs),[6] and nanoparticles (metallic and non-metallic),[7] among others, have been widely synthetized and applied in several area. In nanomedicine, more specifically, the literature shows that nanoscale materials have shown numerous advantages, including unravelling and/or treating human diseases.[8] In theory, due to unique optical properties, relative stability, high brightness, high quantum yield, biocompatibility, and biodegradability,[9] some nanomaterials can be used as promising tools to assist in the generation of bioimages,[2] diagnosis,[10] and treatments of human diseases (Figure 1).[11]

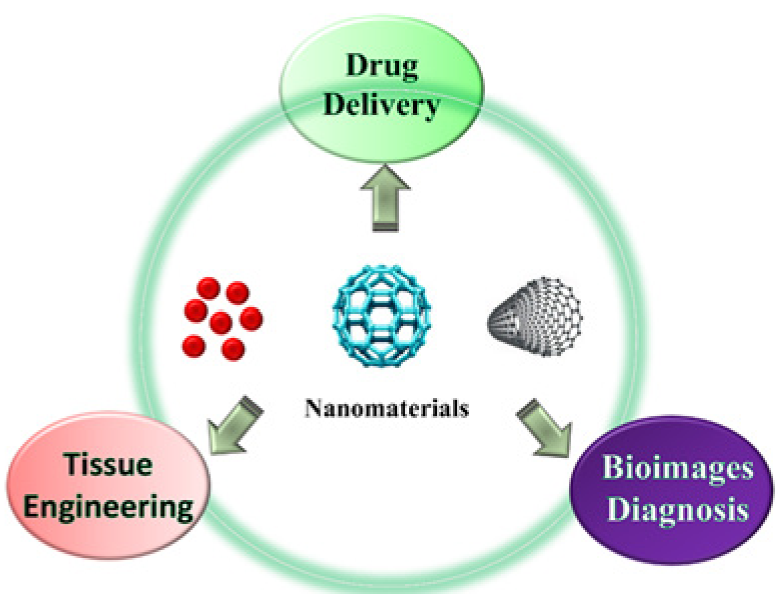

Figure 1. General use of nanomaterials in clinical applications.

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To guarantee specific interactions between nanoparticles and cells, the adsorptive properties of nanomaterials are altered by the selective functionalization of the particles, allowing different clinical applications.[8] For example, Zhang et al.[12] reported a new method for cancer identification called multiplexed nanomaterial-assisted laser desorption/ionization for cancer identification (MNALCI). In this study, Au/SiO_2 core/shell nanoparticles were used as the nanostructured material. The MNALCI was applied to 1,183 subjects, including 233 healthy controls and 950 patients with different types of cancer from two independent cohorts. MNALCI demonstrated a sensitivity of 93% to 91% to distinguish cancers from healthy controls. Satisfactory accuracy and minimal sample consumption make MNALCI a promising solution for non-invasive cancer diagnosis. In another study, magnetic NPs (MNPs), combined with oligomer-specific antibodies targeting neurotoxic beta-amyloid oligomers (AβOs), were evaluated *in vitro* and *in vivo* for imaging neurodegenerative diseases.[2] Furthermore, nanocomposites (natural or synthetic) have been used as nanocarriers to carry out controlled drug delivery to target regions and even for reconstitution of necrotic tissues (tissue engineering).[11,13]

However, the lack of adequate techniques to detect and characterize nanomaterials has exacerbated concerns about the potential risk of using nanomaterials in clinical applications, as the properties of nanomaterials depend on controlling size, shape, specific functional group, and synthesis conditions.[3,8,14] Therefore, more studies are needed to develop an adequate, reproducible, and validated method that allows for the synthesis and characterization of safe nanomaterials for medical practices. In general, there are at least three major challenges regarding nanomaterials production with a focus on nanomedicine.[8,14,15] The first is associated with the development of easy and efficient methods for the large-scale production of high-quality and safe nanomaterials.[14] In other words, although several syntheses are reported in the literature, many of them have low yield, making large-scale production difficult. The second challenge reflects the concern to control the size and shape of particles. Many physicochemical properties of the nanomaterials change with increasing or decreasing size, and therefore the pattern of toxicity may also change.[9] In general, some particle properties vary with decreasing particle size due to surface energy impacts. For example, the properties of metallic particles change when they are smaller than 5 nm. In the literature, there are few studies that report on the toxicity patterns of nanomaterials or the physicochemical properties that are impacted by size variation. For example, the energy levels of QDs are examples of changes in the properties of particles that suffer due to size variation.

Finally, the third challenge is associated with the stability and functionalization of nanomaterials.[14] Aggregation into nanoparticles in solution occurs when physical processes bring the surfaces of particles into contact with each other. The short-range thermodynamic interactions allow bonding between the particles and, consequently, the aggregation. For particles below 100 nm in size, Brownian diffusion controls the long-range forces between individual nanoparticles, causing collisions between particles and the resulting aggregation.[14] Aggregation may represent the low stability of the prepared nanomaterials. In this sense, nanomaterials with low stability can be a risk in clinical application due to nanotoxicity.[15] Therefore, the evaluation of the toxicity of nanoscale materials in the field of nanomedicine implies another important challenge, which is the need for highly detailed *in vitro* and *in vivo* studies on nanotoxicity.[9]

Although, important practical challenges are found in nanoscience, there is no doubt that nanostructured materials present considerable opportunities for advances in nanotechnology applied to nanomedicine. Therefore, more studies are needed to develop easy, efficient, reproducible, and validated methods to ensure the applicability of nanomaterials with a low risk of toxicity.

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