

Chapter 11

Up-Converting Nanoparticles: Promising Markers for Biomedical Applications

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ABSTRACT

Up-converting nanoparticles are dielectric crystalline particles doped with rare-earth ions such as Yb^{3+} , Er^{3+} , Tm^{3+} , Ho^{3+} , Nd^{3+} , etc. When excited in infrared, they emit visible radiation. Used as markers, they present significant advantages in comparison to traditional fluorophores: sharp emission lines, superior photostability, resistance to photobleaching, no blinking and lack of toxicity. Infrared radiation is less harmful to cells avoiding tissue degradation, minimizes auto-fluorescence from endogenous biocomponents offering a good signal-to-background ratio and penetrates tissues deeply. In spite of the great advantages of using up-converting nanoparticles for biomedical applications, there are still some limitations. These refer to identification of optimal size suited for specific samples, prevention of aggregation, water stability/dispersibility, optical efficiency and biocompatibility. This chapter reviews principal characteristics of up-converting nanoparticles and issues related to their use in biomedical applications.

INTRODUCTION

Scientists are trying to open new horizons, envisioning new techniques of investigation, but also the new materials with superior performance. In response to these searches has grown nanomedicine, which gives us a positive outlook in the early identification, effective treatment and cost of various diseases, some with high prevalence in the population. Over time, there were created many bridges between nanotechnology and biomedical sciences. A special interest in the field of nanomedicine is the luminescent materials, which are able to transform a certain type of energy into electromagnetic radiation. From the structural point of view, they are made from a matrix in which are embedded the activator component to

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confer the properties of the luminescence. Currently, the use is so wide, that we meet with luminescent materials in everyday activities: street lighting, on the TV screen or computer display. Among luminescent materials, upconverting nanoparticles have numerous applications in various areas of science, such as displays (Yang, Feng, & Jiang, 2005), solar cells (Ivanova & Pellé, 2010; Shalav, Richards, Trupke, Krämer, & Güdel, 2005), lasers (Sandrock, Scheife, Heumann, & Huber, 1997), lighting, paint industry, NIR visualisation. Although so familiar with their use, the international scientific world continues to be attracted to the study of upconversion nanoparticles, because of their use in biomedical field. This chapter reviews principal characteristics of up-converting nanoparticles and issues related to their use in biomedical applications. Main objectives of this chapter were to provide readers recent progress of upconverting nanoparticles, to discuss certain problems, limitations on their use in biological samples, to prospects the future research directions and suggest new applications.

BACKGROUND

In recent years, biomedical imaging applications have greatly expanded since imaging techniques are key elements of research and diagnosis. Fluorescence imaging is one of the most used applications, with the purpose of prevention, diagnosis, and treatment. Fluorescent compounds named fluorophores or fluorochromes are used both *in vitro* and *in vivo* assays, providing increased sensitivity, high spatial and temporal resolution (Rao, Dragulescu-Andrasi, & Yao, 2007), and the possibility of simultaneous use of multiple fluorophores with different properties (multiplexing) (Zijlmans, et al., 1999). Traditional fluorophores currently used for the usual techniques can be fluorescent organic molecules (NADH, Flavin, aromatic amino acids, porphyrins, lipopigments, collagen, and elastin), inorganic compounds with trademark (ethidium bromide, acridine orange, Hoechst, DAPI, FITC, Alexa Fluor, Texas red), quantum dots or fluorescent beads. Their action mechanism is based on single-photon excitation, process that follows Stokes law, according to which the wavelength of the light emitted is always longer than that of the excitation light (Lakowicz, 2006). Phenomenon named down conversion is represented schematically in Figure 1.

Excitation of the fluorophore takes place at low wavelength, and the colour of the fluorophore depends on the wavelength of emitted light (FITC excitation 495 nm, emission 520 nm). In spite of the numerous benefits, techniques of fluorescence based on the phenomenon of down conversion (classical fluorophores) have a number of disadvantages that limit their use in biomedical applications. As the energy produced is lower than that applied, quantum efficiency of these fluorophores is relatively low (Auzel, 2004). The light emitted in all directions with spherical scatter and a significant autofluorescence from biological tissues determines a low signal-to-background ratio requires a dark background to enhance the resolution. The emission spectra of down conversion fluorescent markers often overlap with that of host tissue autofluorescence, thereby generating some false positives that make interpretation of staining outcome difficult (Idris, et al., 2009). The short penetration depth also limits their use for imaging of deep biological tissues (Choy, Choyke, & Libutti, 2003). Using high-energy, long-term irradiation of excitation light (UV-VIS) used for excitation of fluorochromes, determine photo-damage and degrades both fluorescent particles and biological samples (DNA damage and cell death) (le Masne de Chermont,

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