FACILE SYNTHESIS OF FLUORESCENT COPPER NANOCLUSTERS (CuNCs) AND THEIR RADIOLABELLING WITH ^{64}Cu (^{64}CuNCs) FOR CELLULAR IMAGING AND RADIOTHERANOSTIC APPLICATIONS

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Metal NanoClusters (MNCs) are composed of a discrete number of metal atoms, in the range from few up to a few hundred atoms.[1] Fluorescent metal nanoclusters possess a highly desirable combination of properties, including ultra-small size, high biocompatibility, and exceptional photostability, which make them ideal candidates as fluorescent probes for various bio-applications.[2] Among them, copper nanoclusters (CuNCs) present advantages over other MNCs, including their earth-abundant and low-cost precursors. However, the use of CuNCs in biological systems is limited due to their susceptibility to oxidation and by the difficulty to obtain clusters with both ultrasmall size and high colloidal stability.[3] At the same time, for cancer treatment, radionuclides have gained significant attention.[4] The nuclear properties of the Copper-64 (^{64}Cu) radioisotope make it highly suitable as a radioisotope for Positron Emission Tomography (PET) imaging and for internal radiotherapy in cancer treatment.[5] Here, we developed a straightforward, quick, and scalable protocol to produce orange-emitting fluorescent CuNCs, using a synthesized multidentate thiol-based ligand (Cys-PIMA-PEG) and ascorbic acid (Vitamin C) as reducing agent. The as-synthesized CuNCs show a an average diameter of 1.6 ± 0.2 nm, exhibit an orange emission fluorescence, high QY and good photostability. After assessing the biocompatibility, we used the CuNCs for cellular imaging on living cells. Furthermore, by applying the same protocol using radioactive ^{64}Cu precursor, we obtained radio ^{64}CuNCs. Their radiotherapeutic effect in *in vitro* cell model and their possible use as PET tracer agent *in vivo* has been also investigated on a xenograft murine tumor model. To the best of our knowledge, this is the first example of protocol development and application of radio ^{64}CuNCs, composed of only the radionuclide ^{64}Cu and polymer, without any other external elements.

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