Label Free, Nontoxic Cu-GSH NCs as a Nanoplatform for Cancer Cell Imaging and Subcellular pH Monitoring Modulated by a Specific Inhibitor: Bafilomycin A1

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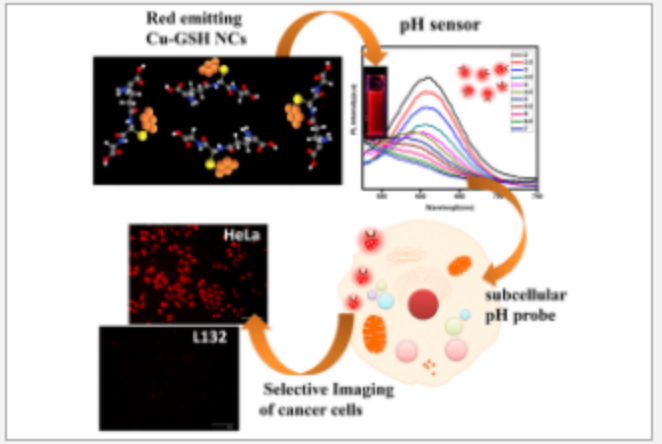
SUBJECTS: Copper, Fluorescence, Nanoparticles, Cells, pH

Abstract

Metal nanoparticles-based sensors invoked much research attention in the biomedical field, especially in applications involving live cell imaging and monitoring. Here, a simple cost-effective method is adopted to synthesize glutathione coated copper nanoclusters (Cu-GSH NCs) with strong bright red fluorescence (625 nm). The clusters were found to be containing five Cu(0) atoms complexed with one molecule of glutathione (GSH) as evidenced by MALDI-TOF MS analysis. The synthesized Cu-GSH NCs system responds linearly to the pH in the acidic and alkaline ranges with a high degree of in vitro pH reversibility, projecting its potential as a real time pH sensor. Higher intensity emission observed in acidic conditions can be exploited for its employability as cellular organelle markers. The imaging and sensing potential of Cu-GSH NCs in the live human adenocarcinoma cell line, the HeLa cells, was tested. The treatment of HeLa cells for 48 h imparted deep red fluorescence, owing to the lower level of intracellular pH in cancer cells. In contrast, the imaging using normal cell lines (L-132, lung epithelial cell line) showed significantly lower fluorescence intensity as compared to that of HeLa cells. The subcellular pH-dependent fluorescence emission of Cu-GSH NCs was further assessed by treating HeLa cells with proton pump (V-ATPase) inhibitor Bafilomycin A1, which increases the vesicular pH. Interestingly, the fluorescent intensity of HeLa cells decreases with increasing concentration of Bafilomycin A1 in the presence of Cu-GSH NCs, as evidenced by the fluorescence microscopic images and quantitative fluorescent output. Accordingly, the developed Cu-GSH NCs system can be employed as an efficient pH-based bioimaging probe for the detection of cancer cells with an implied potential for the label free subcellular organelle tracking and marking. Importantly, the Cu-GSH NCs can be used for live cell pH imaging owing to their high degree of reversibility in sensing of pH variation.



KEYWORDS: Cu GSH nanoclusters, pH sensor, bioimaging, HeLa cells, organelle marker, cancer cell imaging