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ARTICLE

Bio-friendly Maillard reaction fluorescent products from glutathione and ascorbic acid for rapid and label-free detection of Fe^{3+} in living cell

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Developing the probes with good biocompatibility and realizing intracellular detection in living cell are of great significance for biomedical and life science, but remain a challenge now. In this paper, we describe a rapid and highly selective biosensor for Fe^{3+} detection in living cell based on the Maillard reaction fluorescent products (MRFPs) of glutathione and ascorbic acid as a probe. Experiments show that the MRFPs are non-cytotoxic and possess excellent biocompatibility. Moreover, the MRFPs show a rapid response and good selectivity towards Fe^{3+} over other metal ions under physiological pH condition in vitro. The introduction of Fe^{3+} can quench the fluorescence of MRFPs, and the fluorescence intensity of system decreases linearly with increasing concentration of Fe^{3+} in the range of 0.05 – 50 μM with the detection limit of 4.6 nM at a signal-to-noise ratio of 3. Moreover, the recognition mechanism has been discussed, which is attributed to the charge transfer from excited-state MRFPs molecules to metal ions. In addition, the MRFPs have been successfully demonstrated as a good imaging probe for Fe^{3+} sensing in living cells. This study shows that the biocompatible MRFPs might hold great potential application in bioimaging, diagnosis, and therapy of intracellular diseases.

Introduction

It is well known that the free biomolecules and metal ions in vivo cell play important roles in biology by participating in metabolism and maintaining the normal intracellular homeostasis.[1-3] At the same time, it is more effective and meaningful to realize the real-time observation and study on interaction between drug molecules and corresponding targets in living cells.[4-6] Therefore, detection of the content and distribution of free biomolecules and metal ions has significant value in biology and pharmaceutical fields. Because the inherent advantages, including the rapid binding kinetics, easy operation, and ease of automation, the fluorescence assays based on the mechanism of fluorescence resonance energy transfer or charge transfer quenching for targets detection have been widely developed.[7-10] Furthermore, the optical method with fluorescent probes now has been used for intracellular detection due to the advantages of the high sensitivity, in-situ observation (fluorescence imaging technique), and slight cellular damage etc. Recently, various fluorescent probes have been successfully applied in intracellular detection and imaging, including not only the organic fluorescent dyes, but also kinds of quantum dot, inorganic nanoparticles, and fluorescent DNA nanostructures and so on.[11-15] For example, Zhou *et al.* reported an intracellular Pd^{2+} sensor based on the two-photon fluorescent organic molecule as probes;[16] Hu *et al.* described a detection method of Hg^{2+} in living cell with N-acetyl-L-cysteine functionalized CdTe quantum dots as probes;[17] Sharma and coworkers reported the application of fluorescent carbon nanoparticle on intracellular Pd^{2+} and Hg^{2+} sensors;[18] Xiang and coworkers developed a multiplexed sensing platform for microRNAs in living cells based on the reconfigurable DNA nanostructures.[19] However, the wide application of reported intracellular probes has been limited because of some detrimental factors, such as the inevitable cytotoxicity, high-cost, and complex preparation of probes. Therefore, developing new fluorescent probe with good biocompatibility, non-cytotoxicity, and economical, simple and green synthesis route is highly desired for bioimaging, and effective and real-time targets monitoring in living cell.

Maillard reaction is a typical nonenzymatic browning reaction between reducing sugars and amino acids, and Louis-Camille Maillard reported the reaction for the first time in 1912.[20] Because of the widespread existence of Maillard reaction in food and organism, the reaction and associated products have drawn attention from many researchers. Especially, because the corresponding fluorescence emission from the reaction can be used to assess the aging processes of

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food and biological systems, in recent years they have aroused increasingly researchers' interest in food science and biomedical fields.[21-26] Moreover, some Maillard reaction products have been shown to chelate metal ions, and the products from different reaction reagents can be used as chelators of different metal ions.[27] For example, Rendleman demonstrated that Maillard reaction products of fructose and glycine are an effective Ca^{2+} chelator;[28] Rendleman and Inglett further discovered that the products from glucose and glycine Maillard reaction can chelate Cu^{2+};[29] Hashiba's study showed that the Maillard reaction products of maltol and 4-hydroxy-2,5-dimethyl-3(2H)-furanone are associated with Fe^{3+} binding.[30] Moreover, our previous study showed that the Maillard reaction fluorescent products (MRFPs) of glutathione (GSH) and ascorbic acid (AA) can be used as a probe to detect Hg^{2+} under acidic condition (pH 4.1). The principle is based on the fluorescence quenching caused by interaction between the MRFPs and Hg^{2+}, and in the report, we hold that the MRFPs are expected to be a novel fluorescent probe and serve the development of analytical chemistry.[31] However, the biocompatibility and cytotoxicity of the MRFPs have not been evaluated, and the application of MRFPs in bioimaging and intracellular detection has not been explored.

In this work, we carried out the cell toxicity test of the MRFPs from GSH and AA using the human cervical carcinoma cells (Hela cells) in vitro by cell culture method, and the results showed that the MRFPs are non-cytotoxic and biocompatible, which illustrate that the MRFPs can be a potential bioimaging probe and be used for monitoring biomolecules and ions in living cell. Furthermore, the experiments showed that the MRFPs could specifically recognize Fe^{3+} under physiological condition (pH 7.0, 37 °C), and the other metal ions have almost no effects on the results. The fluorescence of system can be quickly quenched when the Fe^{3+} is added, and the quenching efficiency possesses a good linear relation with Fe^{3+} concentration from 0.05 to 50 μM with the detection limit of 4.6 nM at a signal-to-noise ratio of 3. In addition, it has been demonstrated that the MRFPs of GSH and AA can be successfully utilized for Fe^{3+} detection and imaging in living cell. Accordingly, the fluorescent products obtained from Maillard reaction can be used as a good bioprobe for intracellular detection, and the Maillard reaction may be a potentially effective approach to seeking and developing novel fluorescent probes for bioimaging and biosensing fields owing to the selective recognition of different metal ions by different Maillard reaction products.

Materials and methods

Materials and apparatus

L-glutathione (GSH, > 98 %), L-ascorbic acid (AA, > 99 %), and Tris(hydroxymethyl)aminomethane (Tris, > 99 %) were purchased from Aladdin Reagent Co., Ltd., China. All of the metal ions involved in this work were corresponding nitrates and purchased from Chengdu Kelong Chemical Reagents Factory (China). The human cervical carcinoma cells (Hela cells) were obtained from the Chinese Academy of Sciences (Shanghai, China). Fetal bovine serum (FBS), penicillin, and streptomycin were purchased from Thermo Fisher Scientific (USA). The Cell Counting Kit-8 (CCK-8) and other cell culture products used for this experiment were obtained from Nanjing KeyGen Biotech. Inc. (Jiangsu, China). All solutions were freshly prepared, and all the reagents were of analytical reagent grade. Ultrapure water (18.2 MΩ cm) was used throughout the experiments.

The fluorescence and UV–vis absorption spectra were recorded with an F-2700 fluorescence spectrophotometer (Hitachi, Japan) and a UV-2450 spectrophotometer (Shimadzu, Japan), respectively. The slit widths of 10/10 nm for excitation and emission and a photomultiplier tube voltage of 400 V were used for the fluorescence measurements. The Fourier transform infrared (FT-IR) spectrum was taken with a Bruker IFS (Germany) 113v spectrometer after pelleting the fine powder with KBr. Fluorescence lifetime spectrum was obtained on an FLsp920 fluorescence lifetime and steady state spectrometer (Edinburgh, UK). A Bio-Rad 680 microplate reader (USA) was used to obtain the absorbance in the CCK-8 assay. The confocal laser scanning microscope (CLSM) images were obtained with an FV1200 confocal laser scanning microscope (Olympus Optical Co., Ltd.).

Preparation of the Maillard reaction fluorescent products

According to our previous report,[31] the purified MRFPs were prepared as following method: Firstly, 350 μL of 200 mM GSH and 100 μL of 500 mM AA solutions were added to 280 μL of ultrapure water, and the mixture was homogenized by stirring for 1 min. Then 270 μL of 1 M NaOH was added to the above solution with stirring for 1 min; Secondly, the above mixture were stored in 95 ℃ water for 42 h to carry out the Maillard reaction; Finally, and the solution after reaction was centrifuged at 13000 rpm for 30 min, and the supernatant was collected and used for obtaining the purified MRFPs with a silica gel thin-layer chromatography method.[27] The purified MRFPs were stored in a dry container and used directly for all experiments in this work.

Detection of Fe^{3+}

Typically, 20 μL of 1 mg mL^{-1} MRFPs solution and various volumes of $Fe(NO_3)_3$ solutions (1 mM) were added to a certain amount of Tris-HCl buffer (pH 7.0), and the final solution volume was maintained at 1 mL (concentration of MRFPs is 0.02 mg mL^{-1}). The above solutions were then mixed fully and incubated for no less than 20 s at 37 °C with a water bath. Finally, the fluorescence spectra of above solutions were recorded in the wavelength range of 380 to 570 nm.

Cell viability assay

The cytotoxicity of the MRFPs was evaluated with a standard CCK-8 assay. Briefly, 1×10^4 and 5×10^4 cells/well were seeded in 96-well plates with a total volume of 1000 μL/well, and the plates were maintained under the condition of 5% CO_2 at 37 °C for 24 h. After cell attachment, the cells were incubated at different concentrations of MRFPs (0, 0.1, 2.5, 5, 10, 50, 100, 250, 500, 1000 μg mL^{-1}) for 24 h, respectively. Then the cells were washed with phosphate buffer saline (PBS) for three

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times. Then, 10 μL of CCK-8 solution was added to each well and the cells were incubated for another 2 h. Finally, the absorbance was measured at 450 nm with a Bio-Rad 680 microplate reader.

Imaging assay of Fe^{3+} in living cells

The Hela cells (5×10^4 cells/well) were seeded in a 35 mm^2 laser confocal microscopy petri dish with 10 mm well and cultured in DMEM cell culture medium supplemented with 10 % heat-inactivated FBS, 2 mM glutamine, 100 U mL^{-1} penicillin, and 100 U mL^{-1} streptomycin at 37 °C under a humidified condition of 5 % CO_2 for 24 h. Then, the cell culture medium containing 1 mg mL^{-1} MRFPs was used to replace the original cell culture medium, and the Hela cells were incubated for 1 h to make sure that the MRFPs had entered into cells. Subsequently, the cells were washed three times with DMEM to remove the remaining MRFPs. The experiment to assess Fe^{3+} was performed by incubating the cell with cell culture medium containing 10 mM Fe^{3+} for another 30 min to allow sufficient Fe^{3+} uptake and the intracellular fluorescence quenching caused by interaction between Fe^{3+} and MRFPs. Finally, the fluorescence images were acquired with a CLSM, and the excitation wavelength was 405 nm.

Results and discussion

Preparation and characterization of the Maillard reaction fluorescent products

In this paper, the purified MRFPs of GSH and AA have been obtained according to the previous method.[31] The yellowish powder of purified MRFPs is observed under visible light, and shows strong blue emission under UV light, as shown in Fig. S1 (ESI†). At the same time, the maximum excitation and emission wavelengths of the purified MRFPs solution are located at 380 and 450 nm, respectively, and no obvious absorption peak appears within the range of 300 – 450 nm in the UV-vis absorption spectrum of the purified MRFPs solution (concentration of MRFPs is 1 mg mL^{-1}), as shown in Fig. 1. In addition, the photographs of the solution show that the purified MRFPs solution is almost colorless under visible light, and the solution also has a blue emission under UV light (insets in Fig. 1). The above results show the purified MRFPs in this work possess the typical spectral characteristics of Maillard reaction products, for example, the excitation wavelength is located at 340–370 nm and the emission wavelength is located at 420–470 nm.[32]

In addition, Fig. S2 (ESI†) shows the FT-IR spectrum of the purified MRFPs. The peaks located at about 3400, 1621, and 1417 cm^{-1} can be ascribed to the characteristic absorption bands of amino and carboxyl groups, especially for the peak at 1417 cm^{-1}, it corresponds to the flexural vibration modes of –OH in –COOH,[33-35] indicating that the MRFPs contain many amino and carboxyl functional groups.

Cellular toxicity assay of the Maillard reaction fluorescent products

Biological toxicity of probes is a critical factor and determines whether the probes are possible to serve biological and medical fields, therefore, evaluation of biological toxicity of the newly developed probes is very important for the further study. In view of the extensive existence of the Maillard reaction in organism, the MRFPs might have lower toxicity and possess good biological compatibility. To explore the biological toxicity of the MRFPs, the cytotoxicity assay of the MRFPs to Hela cells has been demonstrated based on the CCK-8 test, and the cell viability was used for assessing the cytotoxicity and has been calculated according to the reported method,[36] and the relevant calculation method has been shown in the Supporting Materials. As shown in Fig. 2a, the results indicate that Hela cells of two different concentrations both can normally grow up when treated with 0.1-1000 μg mL^{-1} MRFPs for 24 h, and the cell viability is higher than 100 %. Moreover, the MRFPs can enter Hela cells without any transfection agents, and the cells will excrete MRFPs with the metabolism. The observed results with CLSM showed that the fluorescence emission from cells increased over time after adding the MRFPs to the culture medium. The fluorescence intensity of cells could reach the maximum after 60 min, and the strong emission could keep stable for about 40 min, then the blue fluorescence from cells decreased gradually with the excretion of the MRFPs from cells, and the fluorescence of cells ultimately disappeared after treating the cells with MRFPs for about 150 min. Fig. 2b shows the CLSM images of the cells when treated with the MRFPs for 0, 60, and 150 min, illustrating that the MRFPs have no effect on the morphology of cells. The above results show the MRFP of GSH and AA is non-cytotoxic and have good biocompatibility, and which is expected to be used as a fluorescent probe for intracellular detection and bioimaging.

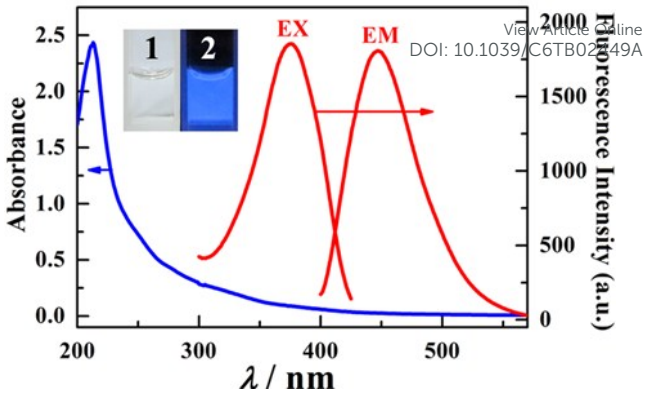

Fig. 1 Fluorescence and UV-vis absorption spectra of purified MRFPs solution. Insets are the photographs of purified MRFPs solution under visible light (no. 1) and UV light (no. 2), respectively. Concentration of MRFPs solution is 1 mg mL^{-1}.

Selective and sensitive detection of Fe^{3+} in vitro

Considering that the strong fluorescence emission from cell can keep constant only about 40 min after the MRFPs of GSH and AA enter the cells, the MRFPs may be more suitable to develop the rapid detection of targets in living cell. At the same time, because of the good response of Maillard reaction products to metal ions, the MRFPs of GSH and AA are considered as intracellular metal ions probes. The recognized

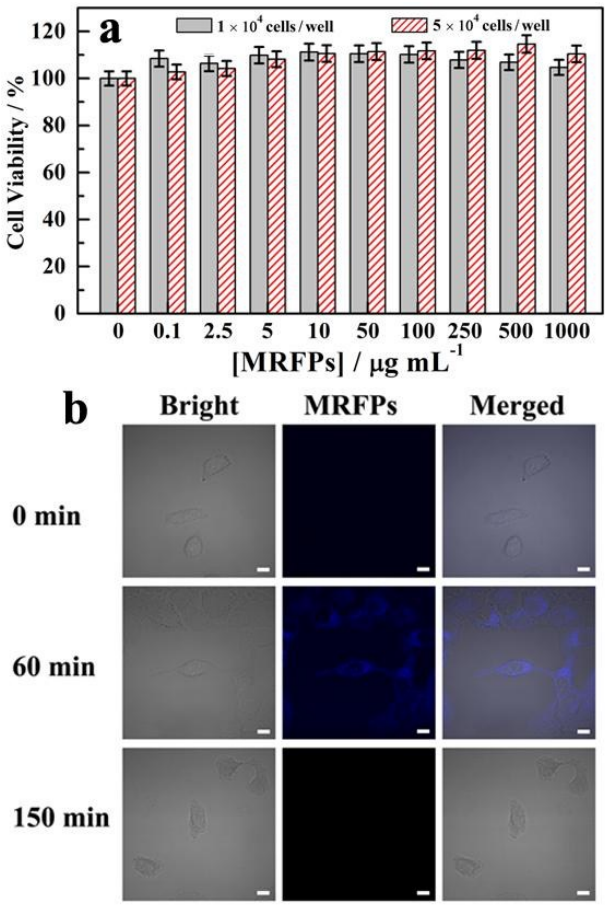

Fig. 2 (a) Cell viability test of Hela cells with two different concentrations treated with various concentrations of the MRFPs (from 0 to 1000 μg mL^{-1}) for 24 h. Concentrations of Hela cells are 1 × 10^4 (solid, left histogram) and 5 × 10^4 (slash, right histogram) cells/well, respectively. (b) CLSM images of the cells when treated with 1 mg mL^{-1} MRFPs for 0, 60, and 150 min, respectively. Scale bar is 10 μm.

ability of the MRFPs to metal ions has been first explored in Tris-HCl buffer (pH 7.0) with water bath of 37 °C, and 14 metal ions (including K^+, Na^+, Ca^{2+}, Mg^{2+}, Ba^{2+}, Pb^{2+}, Ni^{2+}, Al^{3+}, Co^{2+}, Zn^{2+}, Hg^{2+}, Cu^{2+}, Fe^{2+}, and Fe^{3+}) in living cell were selected to react with the MRFPs as targets. The fluorescence quenching efficiency ((F_0 − F) / F_0) is used to assess the recognized ability of MRFPs to targets when the metal ions were added to the system, where F_0 and F are the fluorescence intensities of the system solutions in the absence and presence of various metal ions. The results are shown in Fig. 3a, indicating that most of the metal ions are insensitive to the blue emission of MRFPs under experimental condition. The result shows that only Fe^{3+} can quench the fluorescence at lower concentration (50 μM), and Pb^{2+}, Al^{3+}, Co^{2+}, and Hg^{2+}, and Fe^{2+} can quench slightly the fluorescence at higher concentrations (500 μM for Pb^{2+} and Al^{3+}, 300 μM for Co^{2+}, Hg^{2+}, and Fe^{2+}), however, the Cu^{2+} caused a slight fluorescence quenching at same concentration level to Fe^{3+}. Fig. 3b describes a schematic diagram of fluorescence response of the MRFPs to metal ions.

Although the Cu^{2+} showed a slight fluorescence quenching on the system, the response of the MRFPs to Fe^{3+} is much more sensitive than that to Cu^{2+}. Furthermore, the linear responses of the MRFPs to various concentrations of Fe^{3+} and Cu^{2+} have been investigated under experimental conditions, as shown in Fig. 4 and Fig. S3 (ESI†). The results show that the linear response range is 0.05-50 μM for Fe^{3+} and 1-100 μM for Cu^{2+}. Moreover, the ((F_0 − F) / F_0) of Fe^{3+} to the MRFPs can reach 70 % at the concentration of 50 μM (in the linear range), whereas the ((F_0 − F) / F_0) of Cu^{2+} can only reach about 25 % at the concentration of 100 μM. Accordingly, the MRFPs can be utilized as a fluorescent probe to detect Fe^{3+} with high selectivity compared to many of published Fe^{3+} sensors, in which the detection of Fe^{3+} suffers from the obvious interference of some general metal ions, such as Fe^{2+}, Cu^{2+}, Al^{3+}, and so on.[37-39] In addition, the detection limit for Fe^{3+} is calculated to be 4.6 nM at a signal-to-noise ratio of 3. The effect of reaction time of the system for detecting Fe^{3+} has been studied, as shown in Fig. S4 (ESI†). The result shows that

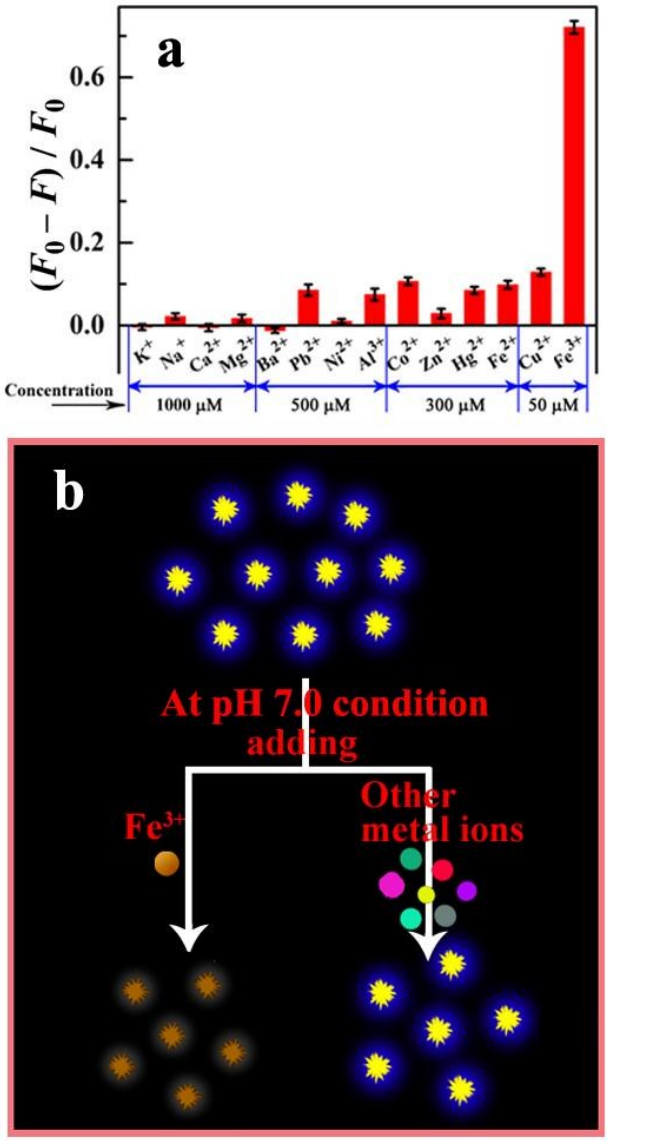

Fig. 3 (a) Fluorescence quenching efficiency of MRFPs in the presence of different metal ions: K^+, Na^+, Ca^{2+}, and Mg^{2+} (1000 μM), Ba^{2+}, Pb^{2+}, Ni^{2+}, and Al^{3+} (500 μM), Co^{2+}, Zn^{2+}, Hg^{2+}, and Fe^{2+} (300 μM), and Cu^{2+} and Fe^{3+} (50 μM). Concentration of MRFPs is 0.02 mg mL^{-1}. (b) Schematic diagram of fluorescence response of the MRFPs to metal ions.

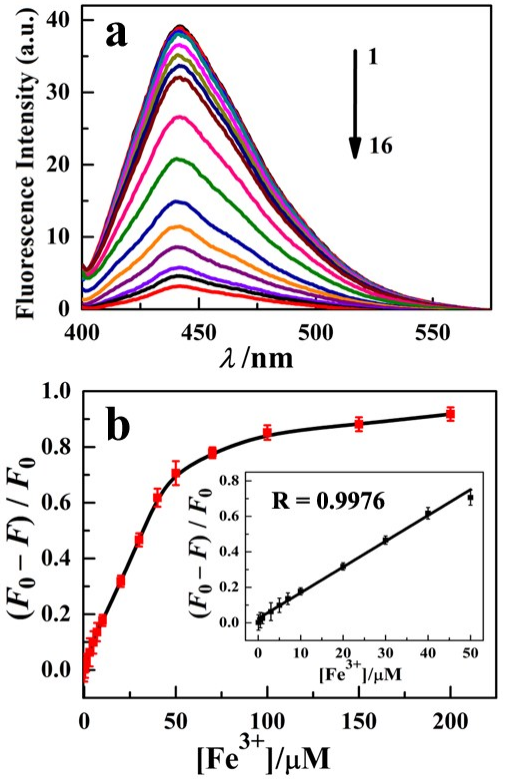

Fig. 4 (a) Fluorescence spectra of the MRFPs in the presence of various concentrations of Fe^{3+} (no.1-16: 0, 0.05, 0.5, 1, 3, 5, 7, 10, 20, 30, 40, 50, 70, 100, 150, 200 μM). (b) Corresponding plots of the values of $((F - F_0) / F_0)$ at 450 nm versus the concentrations of Fe^{3+}. Concentration of MRFPs is 0.02 mg mL^{-1}.

the Fe^{3+} can quench the fluorescence of MRFPs within 3 min, and the fluorescence intensity of the solution and fluorescence quenching efficiency can keep stable for at least 2 h. At the same time, the rapid fluorescence quenching of MRFPs by Fe^{3+} is demonstrated with a videography in the Supporting material, showing the fact that the completed reaction between MRFPs and Fe^{3+} can be realized within 20 s. Thus, the MRFPs are potentially used as an imaging probe to rapidly and selectively detect intracellular Fe^{3+}.

Possible mechanism for the recognition of Fe^{3+}

The possible mechanism for the highly selective recognition of Fe^{3+} by the MRFPs has been investigated in this work. The FT-IR spectrum of the MRFPs (Fig. S2, ESI†) shows that the MRFPs contain many amino and carboxyl functional groups. As is well-known, both the amino and carboxyl groups are strong electron donors, at the same time, the Fe^{3+} is strong electron-deficient, so it is easy to cause the charge transfer from MRFPs to Fe^{3+} when Fe^{3+} was added to the system. On the other hand, according to the well-known activity order and the standard electric potential of metal ions, the electron accepting ability of Cu^{2+} ($\varphi^{\theta}(Cu^{2+}/Cu)$ = 0.345 V) is just behind that of Fe^{3+} ($\varphi^{\theta}(Fe^{3+}/Fe^{2+})$ = 0.770 V), thus the Cu^{2+} can also lead to the fluorescence quenching of MRFPs compared to other metal ions, but the quenching efficiency of Cu^{2+} is less than that of Fe^{3+}, illustrating that Cu^{2+} possesses less effective fluorescence quenching owing to weaker electron accepting ability than Fe^{3+}, which supports the fluorescence quenching mechanism of charge transfer from MRFPs to metal ions. Moreover, although Hg^{2+} ($\varphi^{\theta}(Hg^{2+}/Hg)$ = 0.7973 V) has stronger electron accepting ability than Fe^{3+}, the Hg^{2+} is easily hydrolyzed at high pH medium and the hydrolysis effect can significantly reduce the electron accepting ability of Hg^{2+}. According to our previous study,[31] when pH > 4.56, the quenching efficiency of MRFPs caused by Hg^{2+} would gradually decline, therefore, the Hg^{2+} does not play an effective quencher of MRFPs at pH 7.0 condition. Accordingly, the MRFPs can recognize specifically Hg^{2+} at pH 4.1 and Fe^{3+} at pH 7.0, respectively, which illustrates that the pH value plays a significant role in the recognition ability and sensitivity of the system.

In addition, to further verify the above quenching mechanism, the UV-vis absorption and time-resolved fluorescence spectra of the system have been performed. Fig. 5a shows that no new absorption band appears in the UV–vis absorption spectrum of the system after addition of Fe^{3+}, indicating that the Fe^{3+}-induced fluorescence quenching of MRFPs is not the static quenching.[40] Fig. 5b shows that the fluorescence lifetime of the system decreased from 4.78 to 3.39 ns after addition of Fe^{3+} into the solution. The great reduction of the fluorescence lifetime reveals the occurrence of dynamics quenching, which shows that there is a charge transfer process in the Fe^{3+} sensing system.[41] Combined with the fact that the fluorescence quenching efficiency of metal ions to MRFPs is closely related to the electron accepting ability of metal ions, we attribute the

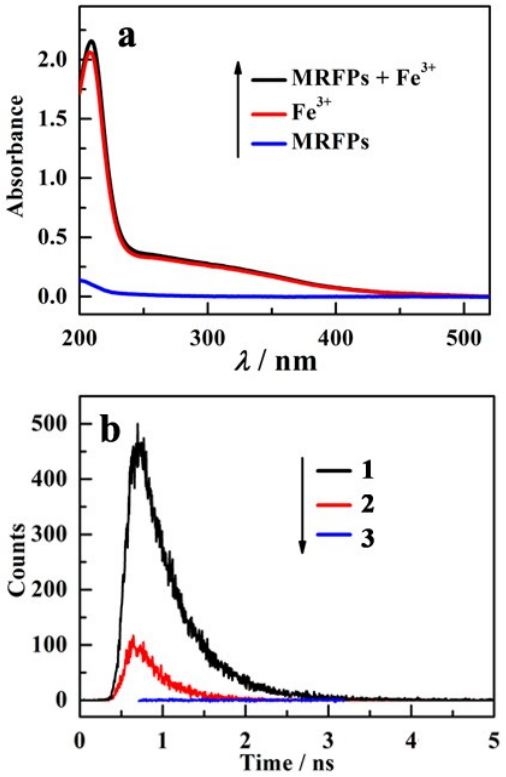

Fig. 5 (a) UV-vis absorption spectra of the MRFPs, Fe^{3+}, and MRFPs + Fe^{3+}. (b) Fluorescence decays of the MRFPs in the absence (curve 1) and presence of Fe^{3+} (curve 2), and curve 3 is weighted residuals time scan curve. Concentrations of MRFPs and Fe^{3+} are 0.02 mg mL^{-1} and 100 μM.

selective and sensitive recognition of Fe^{3+} by the MRFPs to the charge transfer from MRFPs to target in this work.

Intracellular Fe^{3+} sensing

As an important metal ion involved into various biochemical processes in organisms, Fe^{3+} plays an obligatory role in maintaining normal intracellular homeostasis in living cells,[42,43] and the deficiency or excess of Fe^{3+} can lead to a series of disorders. Therefore, developing intracellular Fe^{3+} sensor has important significance for biology and medical research. Although numerous studies on Fe^{3+} detection in living cells have been published,[37,38,44] the safety and selectivity of fluorescent probes are always challenging issues for real-time detection of Fe^{3+} in vivo.

In view of the good biocompatibility and high selectivity of the MRFPs toward Fe^{3+} over other metal ions, the intracellular Fe^{3+} detection with the MRFPs as the probe has been demonstrated based on the CLSM. As shown in Fig. 6, compared to the control experiments, a strong blue-emitting state was observed in Hela cells after treated with MRFPs, and intracellular fluorescence fades when the exogenous Fe^{3+} is introduced into the fluorescent cells. The experimental result indicates the feasibility of the MRFPs for bioimaging and Fe^{3+} detection in living cells. Moreover, the times required for Fe^{3+} uptake and intracellular fluorescence quenching has been explored based on CLSM technique, as shown in Fig. S5 (ESI†), the result shows the process from the addition of Fe^{3+} to the culture medium to obvious fluorescence quenching needed about 20 min, then the complete fluorescence quenching of MRFPs by Fe^{3+} could be observed within 7 min in living cells. The above results show that the MRFPs of GSH and AA can be used as a fluorescent probe for not only real-time bioimaging but also rapid and label-free detection of Fe^{3+} in living cells.

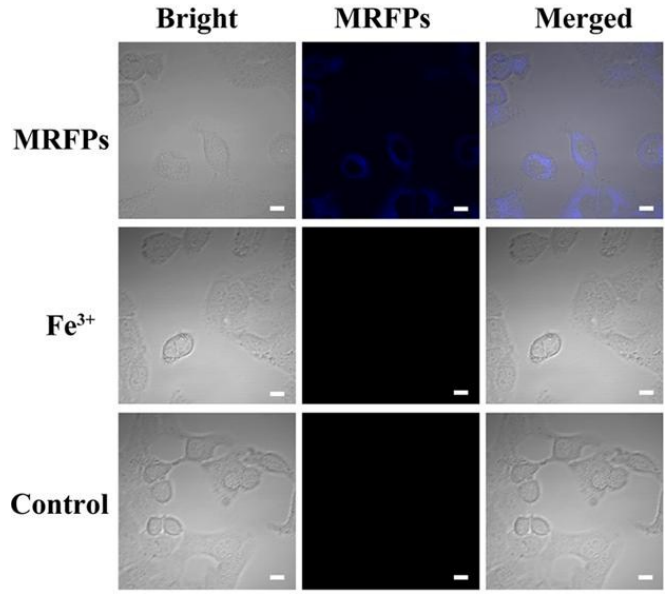

Fig. 6 CLSM images of Hela cells after 1 h incubation with cell culture medium containing 1 mg mL^{-1} MRFPs, and then incubated with cell culture medium containing 10 mM Fe^{3+} for 30 min, respectively. Control experiment was performed by incubating Hela cells with only cell culture medium. Scale bar is 10 μm.

Conclusions

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In conclusion, we have evaluated the cytotoxicity of MRFPs from GSH and AA. The excellent biocompatibility and non-cytotoxicity make MRFPs a more potential bioimaging probe for establishing intracellular sensors. Moreover, the introduction of Fe^{3+} can lead to the fluorescence quenching of MRFPs under physiological conditions (pH 7.0, 37 °C) within 20 s. Based on the sensitive and selective recognition of Fe^{3+} by the bio-friendly MRFPs, the MRFPs of GSH and AA have been utilized as an effective bioimaging probe for rapid and label-free detection of Fe^{3+} in Hela cells. This work provides a valuable reference for the biological safety study of Maillard reaction fluorescent products and demonstrates the significant potential foreground of Maillard reaction products in the fields of biomedicine and life sciences. In addition, the Maillard reactions can provide a new approach to seeking and developing bio-friendly fluorescent probes to serve the progress of biosensor filed.

Acknowledgements

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Bio-friendly Maillard reaction fluorescent products from glutathione and ascorbic acid for rapid and label-free detection of Fe^{3+} in living cell

Jiang Xue Dong, Zi Li Wang, Yue Yang, Zhong Feng Gao, Bang Lin Li, Hui Hui Jiang, Nian Bing Li* and Hong Qun Luo*

The non-cytotoxic Maillard reaction fluorescent products were used as an imaging probe for Fe^{3+} detection in living cells.