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A highly specific and ultrasensitive *p*-aminophenylether-based fluorescent probe for imaging native HOCl in live cells and zebrafish

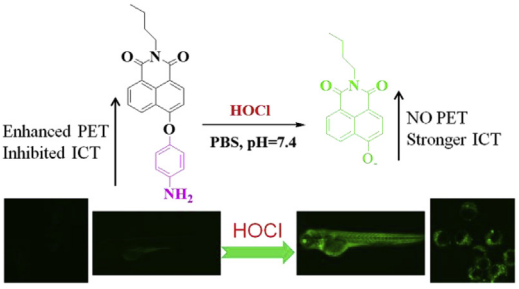
Pan Jia [a], Zihan Zhuang [a], Caiyun Liu [a, **], Zuokai Wang [a], Qingxia Duan [a], Zilu Li [a], Hanchuang Zhu [a], Bin Du [a], Baocun Zhu [a, *], Wenlong Sheng [b, ***], Baotao Kang [c, ****]

[a] School of Resources and Environment, University of Jinan, Shandong Provincial Engineering Technology Research Center for Ecological Carbon Sink and Capture Utilization, Jinan, 250022, PR China
[b] Qilu University of Technology (Shandong Academy of Sciences), Biology Institute of Shandong Academy of Sciences, 19 Keyuan Road, Lixia District, Jinan, 250014, Shandong Province, PR China
[c] School of Chemistry and Chemical Engineering, University of Jinan, Jinan, 250022, PR China

HIGHLIGHTS

- A new *p*-aminophenylether-based fluorescent probe for tracking HOCl was developed.
- The probe could sensitively determine HOCl (DL = 1.37 nM).
- The probe exhibited high selectivity towards HOCl over •OH and $ONOO^-$
- The probe was applied to the visualization of native HOCl in live cells and zebrafish.

GRAPHICAL ABSTRACT



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ABSTRACT

It is very important to detect native hypochlorous acid (HOCl) in the complex biosystems owing to the important roles of HOCl in the immune defense and the pathogenesis of numerous diseases. In this paper, a new *p*-aminophenylether-based fluorescent probe **PAPE-HA** was developed for specific detection of HOCl. Probe **PAPE-HA** could implement the quantitative detection of HOCl ranging from 0 to 1 μM and the detection limit was obtained as low as 1.37 nM. Additionally, probe **PAPE-HA** could reach a rapid response for HOCl (<2 min). Importantly, probe **PAPE-HA** with preeminent specificity and ultrasensitivity was proven to possess powerful capability of tracking native HOCl in live cells and zebrafish, and we thus anticipate that probe **PAPE-HA** could be used as a novel promising tool for revealing diverse cellular functions of HOCl.

1. Introduction

Hypochlorous acid (HOCl), as a vital reactive oxygen species (ROS), is endogenously produced from Cl^- and H_2O_2 under the help of myeloperoxidase in the biosystems [1,2]. Hypochlorous acid plays pivotal roles in immune defense against invading pathogens

* Corresponding authors.
** Corresponding author.
*** Corresponding author.
**** Corresponding author.
E-mail addresses: liucaiyun1982072@163.com (C. Liu), lcyzbc@163.com (B. Zhu), 15618694162@163.com (W. Sheng), chm_kangbt@ujn.edu.cn (B. Kang).

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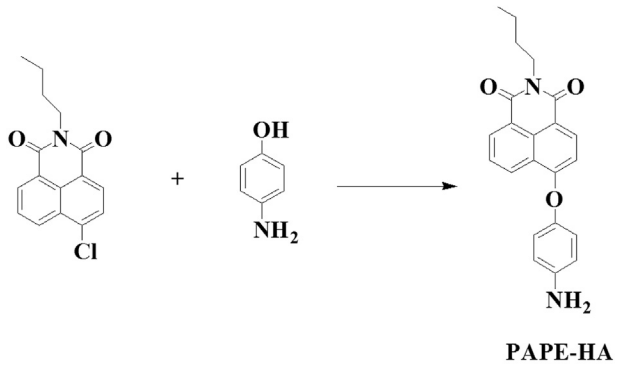
despite its ultra-low concentration in the biological systems [3–5]. However, owing to the high reactivity of HOCl [6–8], excessive production of HOCl can cause a series of diseases closely related to inflammation [9–13]. Therefore, it is very important to establish a satisfactory method for detecting native HOCl in live cells and *in vivo*.

Compared with other traditional methods, small molecule fluorescent probe is known for its outstanding sensitivity and high spatiotemporal resolution in the bioimaging applications [14–16]. Recently, a great many fluorescent probes for monitoring HOCl have been designed based on different recognition receptors [17–44]. Obviously, these fluorescent probes possess some unique merits in many ways, but they still have some limitations including low sensitivity, poor selectivity, and limited bioimaging applications *in vivo*. Consequently, it is still very necessary to construct novel specific and ultrasensitive fluorescent probes for detecting HOCl in live cells and *in vivo*.

4-Hydroxy-1,8-naphthalimide fluorophore with preeminent intramolecular charge transfer (ICT) structure was reported by us for the first time [45], and has been widely applied to the design of fluorescent probes because of its preeminent photophysical performances [46–48]. Additionally, Peng et al. demonstrated that electron-rich moiety could cause an enhanced photo-induced electron transfer (PET) effect to the fluorophore, which is a preferred strategy for constructing highly effective turn-on fluorescent probes [49]. On the other hand, it is reported that *p*-aminophenol moiety could react with highly reactive oxygen species including $^{\bullet}OH$, $ONOO^{-}$, and HOCl [50,51]. Inspired by the reaction mechanism, some *p*-aminophenol-based fluorescent probes employing different fluorophores have been developed for detecting HOCl in the aqueous solution and live cells [42,52,53]. However, *p*-aminophenol-caged D-luciferin has been proven to not respond well to HOCl [22]. Thus, we reasonably envisaged that the reactivity of *p*-aminophenol moiety might be modulated by the bonded fluorophore.

Based on the above considerations, we developed a new 4-hydroxynaphthalimide-derived *p*-aminophenylether-based fluorescent probe **PAPE-HA** for specific and ultrasensitive detection of native HOCl in live cells and *in vivo*. In the design of probe **PAPE-HA**, *p*-aminophenol group with electron-rich was placed at the 4-position of 1,8-naphthalimide (Scheme 1), and the enhanced PET effect and inhibited ICT process should more effectively quench the fluorescence of 4-hydroxy-1,8-naphthalimide fluorophore. As expected, probe **PAPE-HA** with satisfactory water-solubility exhibited very weak fluorescence in the aqueous solution. Further experimental results demonstrated probe **PAPE-HA** possesses many excellent recognition performances, such as high specificity, ultrasensitivity and rapid response. Finally, probe **PAPE-HA** was successfully used for the visualization of native HOCl in live cells and zebrafish.



Scheme 1. The synthesis of fluorescent probe **PAPE-HA** for detecting HOCl.

2. Experimental section

2.1. Materials and instruments

Except for special labels, chemical reagents were obtained from commercial vendor and employed without further purification. High resolution mass spectra (HRMS) were obtained by LC-MS2010A instrument. ^{1}H and ^{13}C NMR data were obtained by Bruker AV-400 NMR spectrometer. Absorption spectra were obtained by UV-3101PC spectrophotometer. Fluorescence spectra were obtained by Horiba FluoroMax-4 spectrophotometer. Fluorescence imaging of HOCl in live RAW 264.7 macrophage cells and zebrafish were carried out on an Olympus FV1000-IX81 confocal fluorescence microscope.

2.2. Synthesis of probe ***PAPE-HA***

N-butyl-4-chloro-1,8-naphthalimide (287 mg, 1 mmol), 4-aminophenol (327 mg, 3 mmol) and Cs_2CO_3 (1.97 g, 6 mmol) were dissolved in acetonitrile solution (14 mL), and then the reaction solution was stirred at 85 °C for 4 h. After cooling down the reaction solution to room temperature, the solvent was disposed by vacuum suction filtration. The resulting solution was evaporated and the residue was further purified with silica column chromatography (dichloromethane containing 1% methanol as eluent) to get the slight yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ ($*10^{-6}$): 0.975 (t, $J = 7.4$ Hz, 3H), 1.401–1.494 (m, 2H), 1.675–1.751 (m, 2H), 3.757 (s, 2H), 4.173 (t, $J = 7.6$ Hz, 2H), 6.782 (d, $J = 8.8$ Hz, 2H), 6.846 (d, $J = 8.4$ Hz, 1H), 6.996 (d, $J = 8.8$ Hz, 2H), 7.764 (t, $J = 8.0$ Hz, 1H), 8.424 (d, $J = 8.4$ Hz, 1H), 8.644 (d, $J = 8.4$ Hz, 1H), 8.718 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ($*10^{-6}$): 13.86, 20.41, 30.27, 40.13, 109.39, 115.92, 116.39, 122.07, 122.60, 123.63, 126.23, 128.60, 129.64, 131.74, 132.95, 144.32, 146.32, 161.01, 163.87, 164.50. HRMS (ESI): Calcd for $C_{22}H_{21}N_2O_3$ $[M+H]^+$ 361.1547; Found, 361.1552.

3. Results and discussion

3.1. Characteristic spectra of probe ***PAPE-HA***

As shown in Fig. 1, probe **PAPE-HA** showed a negligible fluorescence intensity at 557 nm in the phosphate buffered solution (PBS, 5 mM, pH = 7.4). The weak fluorescence of probe **PAPE-HA**

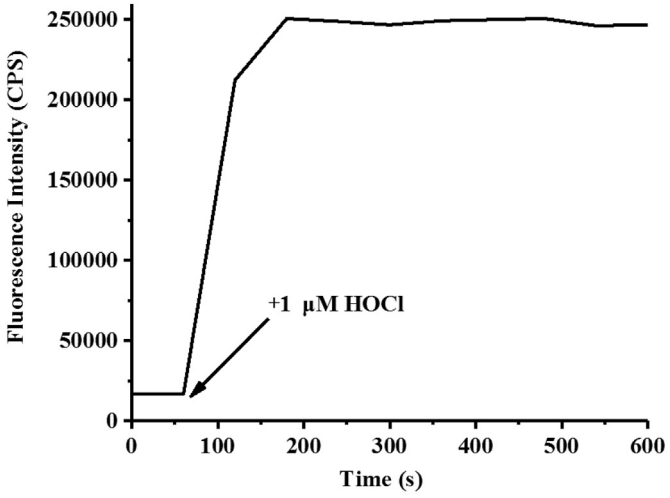
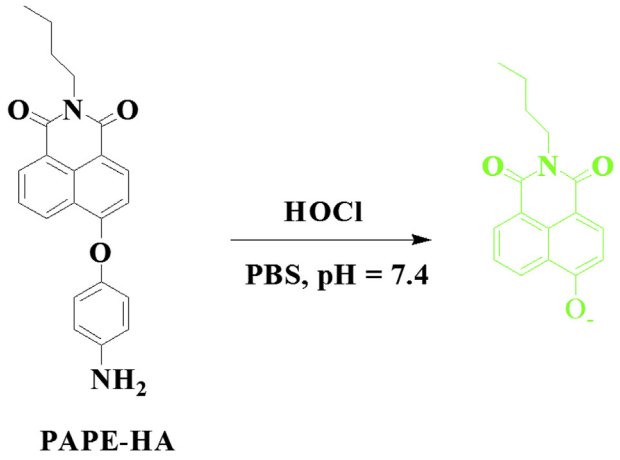


Fig. 1. Time-course of probe **PAPE-HA** (5 μM) for tracking HOCl (1 μM) under the PBS solution (5 mM, pH = 7.4) at 25 °C. $\lambda_{ex} = 468$ nm, $\lambda_{em} = 557$ nm. Slit widths: $W_{ex} = 4$ nm, $W_{em} = 4$ nm.

might be ascribed to the enhanced PET effect and inhibited ICT process (see theoretical calculation in the Supporting Information). In contrast, probe **PAPE-HA** displayed a fast response (<2 min) and the significant fluorescence enhancement by addition of HOCl. The experimental results indicated that probe **PAPE-HA** could offer a rapid and sensitive assay of HOCl in the biosystems. The absorption spectra of probe **PAPE-HA** (20 μM) for detecting HOCl (20 μM) was also investigated (Fig. 2). Probe **PAPE-HA** showed a major absorption peak at 375 nm and an obvious absorption peak at around 455 nm was obtained upon addition of HOCl. The prominent fluorescence enhancement and red-shifted absorption spectra demonstrated the generation of strong ICT structure [43]. To further confirm the reaction mechanism of probe **PAPE-HA** and HOCl, the fluorescent reaction product was characterized to be 4-hydroxy-1,8-naphthalimide by HRMS, indicating the HOCl-mediated oxidative removal of *p*-aminophenylether moiety (Scheme 2).



Scheme 2. The response mechanism of fluorescent probe **PAPE-HA** for HOCl.

3.2. Quantification of HOCl

The fluorescence titration experiments were carried out. As shown in Fig. 3a, free probe **PAPE-HA** showed negligible fluorescence intensity at 557 nm, and the fluorescence intensities at 557 nm ascended successively upon the continuous addition of HOCl (0–5 μM). Moreover, fluorescence intensities at 557 nm increased linearly in the presence of (0–1 μM) HOCl (linear equation: $y = 212821 \times [\mathrm{HOCl}]\ (\mu M) + 20527$, $R^2 = 0.9928$). The above data illustrated that probe **PAPE-HA** could be applied to detect HOCl at the nanomolar level (Fig. 3b). The detection limit was also obtained as 1.37 nM (3σ/k). Consequently, probe **PAPE-HA** possessed the property of ultrasensitivity (Table 1 and S1).

3.3. Selectivity of probe *PAPE-HA* towards HOCl

The high selectivity of probe **PAPE-HA** towards HOCl was investigated carefully by fluorescence spectra. Probe **PAPE-HA** displayed a specific detection of HOCl over other analytes, such as K^+, Ca^{2+}, Na^+, Mg^{2+}, Zn^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Co^{2+}, F^-, I^-, PO_4^{3-}, ATP, NO_3^-, NO_2^-, Cl^-, SO_3^{2-}, HSO_3^-, SO_4^{2-}, S^{2-}, cysteine (Cys), homocysteine (Hcy), glutathione (GSH), H_2O_2, *tert*-butylhydroperoxide (TBHP), O_2^-, hydroxyl radical (•OH), tert-butoxy radical (•O^{t}Bu), $^1O_2$, NO, $ONOO^-$. A remarkable fluorescence enhancement at 557 nm was obtained upon the addition of HOCl, comparatively negligible fluorescence changes were acquired upon addition of other higher concentration analytes (Fig. 4). The results fully manifested the excellent selectivity of probe **PAPE-HA** for detecting HOCl based on the unique recognition receptor of *p*-aminophenylether moiety.

3.4. Bioimaging applications of probe *PAPE-HA* in live cells

Cytotoxicity estimation of probe **PAPE-HA** in live RAW 264.7 macrophage cells by a cell counting kit-8 (CCK-8) assay suggested probe **PAPE-HA** has low cytotoxicity (Fig. S1). Then to explain the application of the probe for tracking HOCl in the complex biosystems, biological imaging of HOCl in live RAW 264.7 macrophage cells was studied (Fig. 5). The control cells presented almost no fluorescence (Fig. 5a and b). The cells preincubated with probe **PAPE-HA** (10 μM) for 20 min showed moderate green fluorescence (Fig. 5c and d). After adding HOCl (10 μM) to the above cells, the significant fluorescence enhancement was observed (Fig. 5e and f). The above experimental results indicated that probe **PAPE-HA** was successfully used to detect exogenous HOCl. Next, to demonstrate the application of endogenous detection for HOCl by probe **PAPE-**

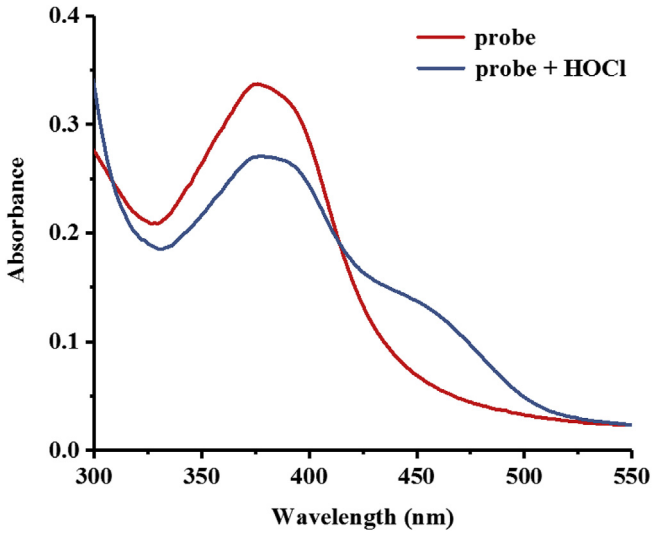


Fig. 2. Absorption responses of probe **PAPE-HA** (20 μM) in the presence of HOCl (20 μM) under the PBS solution (5 mM, pH = 7.4) at 25 °C.

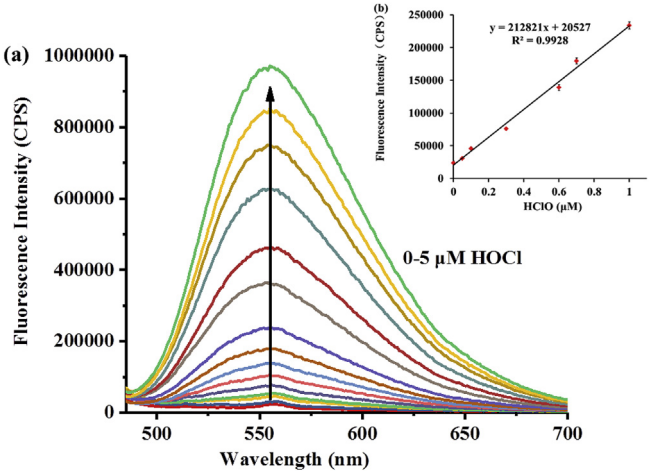
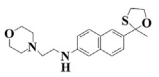
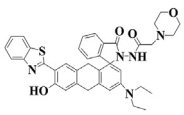
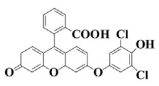
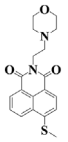
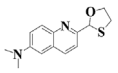
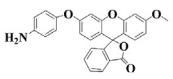
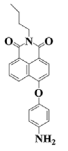


Fig. 3. (a) The fluorescence spectra of probe **PAPE-HA** (5 μM) with the continuous addition of HOCl (0–5 μM) in the PBS solution (5 mM, pH = 7.4). (b) The fluorescence intensities at 557 nm of probe **PAPE-HA** (5 μM) as a function of HOCl concentrations (0–1 μM). $\lambda_{ex} = 468$ nm. Slit widths: $W_{ex} = 4$ nm, $W_{em} = 4$ nm. Each spectrum was recorded 5 min after HOCl addition at 25 °C.

Table 1
Comparison of fluorescent probes for HOCl.

Probes	Solution	Linear range	Detection Limit	Response time	References
	PBS/EtOH, 1:1	0–200 nM	16.6 nM	Within seconds	J. Am. Chem. Soc. 2015, 137, 5930
	30% DMSO	0–50 μM	110 nM	~10 s	J. Mater. Chem. B 2016, 4, 4739
	0.1% DMF	0–10 μM	0.33 nM	1 min	Chem. Sci. 2016, 7, 2094
	aqueous solution	3–150 μM	674 nM	2.5 min	Anal. Chem. 2017, 89, 10384
	5% DMF	0.8–12.5 μM	89 nM	60 s	Chem. Sci. 2018, 9, 6035
	5% EtOH	0.1–1 μM	0.65 nM	~5 min	Chem. Commun. 2018, 54, 3835
	aqueous solution	0–1 μM	1.37 nM	<2 min	This work

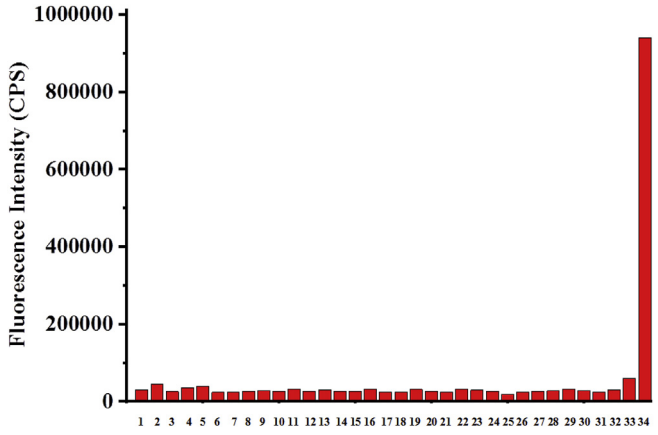


Fig. 4. The fluorescence responses of probe **PAPE-HA** (5 μM) in the presence of various analytes (100 μM except for specific labels) in the PBS solution (5 mM, pH = 7.4). 1. Blank, 2. K^+, 3. Ca^{2+}, 4. Na^+, 5. Mg^{2+}, 6. Zn^{2+}, 7. Cu^{2+}, 8. Fe^{2+}, 9. Fe^{3+}, 10. Mn^{2+}, 11. Co^{2+}, 12. F^-, 13. I^-, 14. PO_4^{3-}, 15. ATP (1 mM), 16. NO_3^-, 17. NO_2^-, 18. Cl^-, 19. SO_3^{2-}, 20. HSO_3^-, 21. SO_4^{2-}, 22. S^{2-}, 23. Cys (500 μM), 24. Hcy (500 μM), 25. GSH (5 mM), 26. H_2O_2, 27. TBHP, 28. O_2^-, 29. •OH, 30. •O^{t}Bu, 31. $^1O_2$, 32. NO, 33. $ONOO^-$ (5 μM), 34. HOCl (5 μM). λ_{ex} = 468 nm. Slit widths: W_{ex} = 4 nm, W_{em} = 4 nm. Bars represent the fluorescence intensities at 557 nm and each spectrum was acquired 5 min after various analytes addition at 25 °C.

HA, the following experiments were carried out. Firstly, the cells preconditioned with phorbol 12-myristate 13-acetate (PMA, a ROS stimulant) were further incubated with probe **PAPE-HA** for 20 min, and they displayed the stronger green fluorescence in cells (Fig. 5g and h). After that, the cells preconditioned with *N*-acetyl-L-cysteine (NAC, a scavenger of HOCl) showed the weaker green intracellular fluorescence (Fig. 5i and j). All these experimental results verified fully that probe **PAPE-HA** could track native HOCl and the fluctuations of endogenous/exogenous HOCl levels in live cells (Fig. 5k).

3.5. Bioimaging applications of probe *PAPE-HA* in zebrafish

Next, the applications of probe **PAPE-HA** in 5-day-old zebrafish were performed (Fig. 6). The zebrafish incubated with probe **PAPE-HA** (10 μM) exhibited a weaker green fluorescence (Fig. 6a and b). Then HOCl (10 μM) was added to the zebrafish, and a bright green fluorescence was observed (Fig. 6c and d). Additionally, the zebrafish pretreated with PMA displayed the stronger green fluorescence than zebrafish only incubated with probe **PAPE-HA** (Fig. 6e and f). Furthermore, the zebrafish preconditioned with NAC exhibited the weaker green fluorescence than zebrafish only incubated with probe **PAPE-HA** (Fig. 6g and h). These results convincingly indicated that probe **PAPE-HA** possessed the high tissue penetration and could realize the visualization of native HOCl and the fluctuations of endogenous/exogenous HOCl levels in zebrafish (Fig. S2).

4. Conclusions

In conclusion, a new 4-hydroxynaphthalimide-derived fluorescent probe **PAPE-HA** was rationally constructed to detect intracellular native HOCl in the biosystems. Probe **PAPE-HA** displayed preeminent selectivity for HOCl over other high concentration analytes due to the use of unique recognition unit of *p*-aminophenylether group. Moreover, bioimaging applications of probe

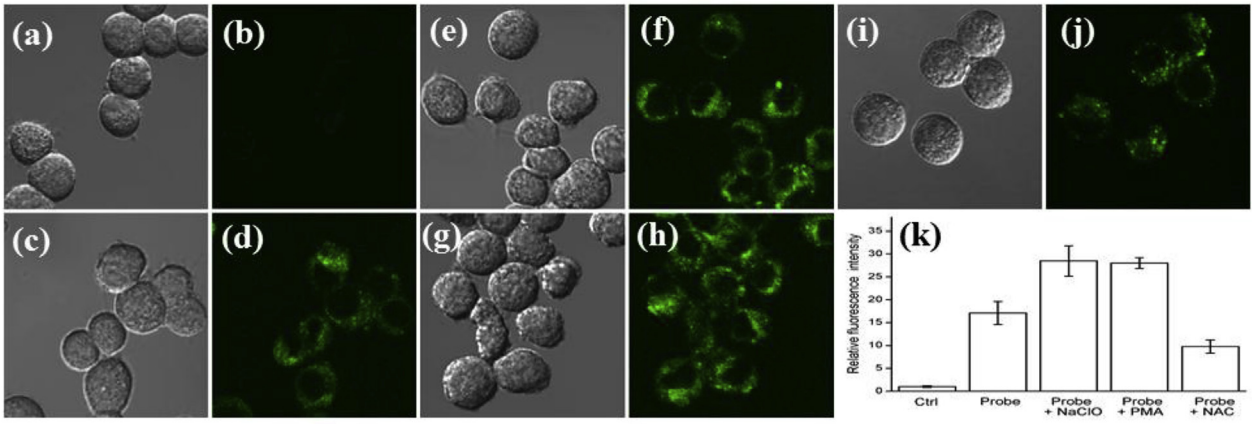


Fig. 5. Fluorescence imaging of HOCl in live RAW 264.7 macrophage cells: (a–b) the control cells; (c–d) the cells incubated with probe **PAPE-HA** (10 μM) for 20 min; (e–f) the cells incubated with probe **PAPE-HA** (10 μM) for 20 min followed by the addition of HOCl (10 μM) for 10 min; (g–h) the cells incubated with probe **PAPE-HA** (10 μM) for another 20 min after preincubation with 1.0 μg mL^{-1} PMA for 60 min; (i–j) the cells incubated with probe **PAPE-HA** (10 μM) for another 20 min after preincubation with 500.0 μM NAC for 60 min; (a, c, e, g, i) the bright-fields; (b, d, f, h, j) the green channels; (k) Bars represent the relative fluorescence intensities between the corresponding cells and control cells. The provided images of live RAW 264.7 macrophage are representative ones (n = 10 fields of cells). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

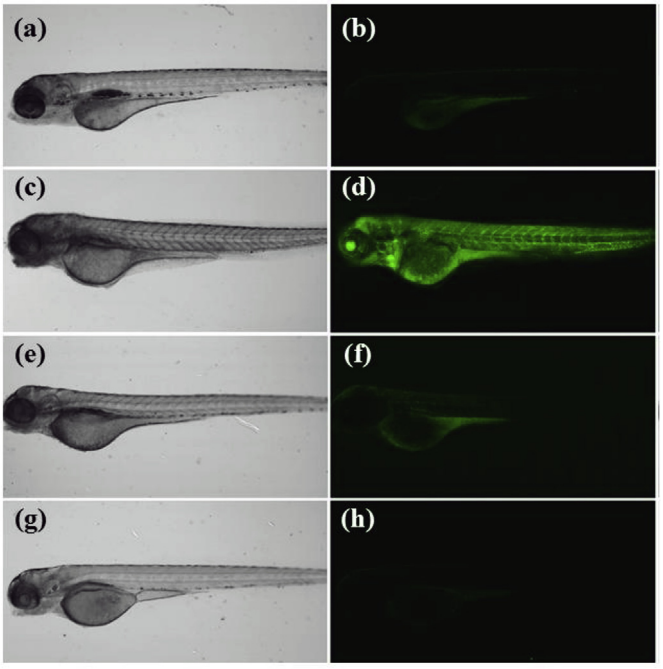


Fig. 6. Fluorescence imaging of HOCl in zebrafish: (a–b) the zebrafish incubated with probe **PAPE-HA** (10 μM) for 20 min; (c–d) the zebrafish incubated with probe **PAPE-HA** (10 μM) for 20 min followed by the addition of HOCl (10 μM) for 10 min; (e–f) the zebrafish incubated with probe **PAPE-HA** (10 μM) for another 20 min after preincubation with 1.0 μg mL^{-1} PMA for 30 min; (g–h) the zebrafish incubated with probe **PAPE-HA** (10 μM) for another 20 min after preincubation with 500.0 μM NAC for 30 min; (a, c, e, g) the bright-fields; (b, d, f, h) the green channels. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

PAPE-HA demonstrated that the probe could visualize native HOCl in live cells and zebrafish. This work not only offers an excellent fluorescent probe with remarkable specificity and ultrasensitivity for detecting intracellular native HOCl in the biological systems, but also further demonstrates that the *p*-aminophenylether moiety would be an ideal recognition receptor of HOCl by combining the preferred fluorophore.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aca.2018.11.031.

References

[1] E.A. Podrez, H.M. Abu-Soud, S.L. Hazen, Myeloperoxidase-generated oxidants and atherosclerosis, Free Radical Biol. Med. 28 (2000) 1717–1725.
[2] Z.M. Prokopowicz, F. Arce, R. Biedron, C.L. Chiang, M. Ciszek, D.R. Katz, M. Nowakowska, S. Zapotoczny, J. Marcinkiewicz, B.M. Chain, Hypochlorousacid: a natural adjuvant that facilitates antigen processing, cross-priming, and the induction of adaptive immunity, J. Immunol. 184 (2010) 824–835.
[3] C.C. Winterbourn, M.B. Hampton, J.H. Livesey, A.J. Kettle, Modeling the reactions of superoxide and myeloperoxidase in the neutrophil phagosome: implications for microbial killing, J. Biol. Chem. 281 (2006) 39860–39869.
[4] D.I. Pattison, M.J. Davies, Absolute rate constants for the reaction of hypochlorous acid with protein side chains and peptide bonds, Chem. Res. Toxicol. 14 (2001) 1453–1464.
[5] B.C. Zhu, L. Wu, M. Zhang, Y.W. Wang, C.Y. Liu, Z.K. Wang, Q.X. Duan, P. Jia, A highly specific and ultrasensitive near-infrared fluorescent probe for imaging basal hypochlorite in the mitochondria of living cells, Biosens. Bioelectron. 107 (2018) 218–223.
[6] N.M. Domigan, T.S. Charlton, M.W. Duncan, C.C. Winterbourn, A.J. Kettle, Chlorination of tyrosyl residues in peptides by myeloperoxidase and human neutrophils, J. Biol. Chem. 270 (1995) 16542–16548.
[7] Y.W. Yap, M. Whiteman, B.H. Bay, Y. Li, F.S. Sheu, R.Z. Qi, C.H. Tan, N.S. Cheung, Hypochlorous acid induces apoptosis of cultured cortical neurons through activation of calpains and rupture of lysosomes, J. Neurochem. 98 (2006) 1597–1609.
[8] Y.C. Yang, H.H. Lu, W.T. Wang, I. Liau, Selective and absolute quantification of endogenous hypochlorous acid with quantum-dot conjugated microbeads, Anal. Chem. 83 (2011) 8267–8272.
[9] B. Zhu, L. Wu, M. Zhang, Y. Wang, Z. Zhao, Z. Wang, Q. Duan, P. Jia, C. Liu, A fast-response, highly specific fluorescent probe for the detection of picomolar hypochlorous acid and its bioimaging applications, Sens. Actuators, B

263 (2018) 103–108.
[10] W.C. Chen, P. Venkatesan, S.P. Wu, A turn-on fluorescent probe for hypochlorous acid based on HOCl-promoted removal of the C=N bond in BODIPY-hydrazone, New J. Chem. 39 (2015) 6892–6898.
[11] L.J. Hazell, L. Arnold, D. Flowers, G. Waeg, E. Malle, R. Stocker, Presence of hypochlorite-modified proteins in human atherosclerotic lesions, J. Clin. Invest. 97 (1996) 1535–1544.
[12] M. Whiteman, P. Rose, J.L. Siau, N.S. Cheung, G.S. Tan, B. Halliwell, J. S, Armstrong, Hypochlorous acid-mediated mitochondrial dysfunction and apoptosis in human hepatoma HepG2 and human fetal liver cells: role of mitochondrial permeability transition, Free Radic. Biol. Med. 38 (2005) 1571–1584.
[13] B.C. Zhu, L. Wu, M. Zhang, Z.Y. Zhao, Z.K. Wang, Q.X. Duan, P. Jia, Z.L. Li, H.C. Zhu, C.Y. Liu, A highly specific and ultrasensitive fluorescent probe for monitoring hypochlorous acid and its applications in live cells, Sens. Actuators, B 267 (2018) 589–596.
[14] K. Xu, D. Luan, X. Wang, B. Hu, X. Liu, F. Kong, B. Tang, An ultrasensitive cyclization-based fluorescent probe for imaging native HOBr in live cells and zebrafish, Angew. Chem. Int. Ed. 55 (2016) 12751–12754.
[15] B.C. Zhu, L. Wu, Y.W. Wang, M. Zhang, Z.Y. Zhao, C.Y. Liu, Z.K. Wang, Q.X. Duan, P. Jia, A highly selective and ultrasensitive ratiometric far-red fluorescent probe for imaging endogenous peroxynitrite in living cells, Sens. Actuators, B 259 (2018) 797–802.
[16] B. Zhu, M. Zhang, L. Wu, Z. Zhao, C. Liu, Z. Wang, Q. Duan, Y. Wang, P. Jia, A highly specific far-red fluorescent probe for imaging endogenous peroxynitrite in the mitochondria of living cells, Sens. Actuators, B 257 (2018) 436–441.
[17] X.Y. Jiao, Y. Li, J.Y. Niu, X.L. Xie, X. Wang, B. Tang, Small-molecule fluorescent probes for imaging and detection of reactive oxygen, nitrogen, and sulfur species in biological systems, Anal. Chem. 90 (2018) 533–555.
[18] X.Q. Chen, F. Wang, J.Y. Hyun, T.W. Wei, J. Qiang, X.T. Ren, I. Shin, J. Yoon, Recent progress in the development of fluorescent, luminescent and colorimetric probes for detection of reactive oxygen and nitrogen species, Chem. Soc. Rev. 45 (2016) 2976–3016.
[19] Y. Yue, F. Huo, C. Yin, J.O. Escobedo, R.M. Strongin, Recent progress in chromogenic and fluorogenic chemosensors for hypochlorous acid, Analyst 141 (2016) 1859–1873.
[20] Y.-R. Zhang, X.-P. Chen, S. Jing, J.-Y. Zhang, Q. Yuan, J.-Y. Miao, B.-X. Zhao, A ratiometric fluorescent probe for sensing HOCl based on a coumarin-rhodamine dyad, Chem. Commun. 50 (2014) 14241–14244.
[21] Y.W. Wang, L. Wu, C.Y. Liu, B.P. Guo, B.C. Zhu, Z.K. Wang, Q.X. Duan, Z.M. Ma, X.L. Zhang, A highly specific and ultrasensitive fluorescent probe for basal lysosomal HOCl detection based on chlorination induced by chlorinium ions (Cl^+), J. Mater. Chem. B 5 (2017) 3377–3382.
[22] C.C. Tang, Y.Q. Gao, T.T. Liu, Y.X. Lin, X.M. Zhang, C.C. Zhang, X. Li, T.C. Zhang, L.P. Du, M.Y. Li, Bioluminescent probe for detecting endogenous hypochlorite in living mice, Org. Biomol. Chem. 16 (2018) 645–651.
[23] L.J. Liang, C. Liu, X.J. Jiao, L.C. Zhao, X.S. Zeng, A highly selective and sensitive photoinduced electron transfer (PET) based HOCl fluorescent probe in water and its endogenous imaging in living cells, Chem. Commun. 52 (2016) 7982–7985.
[24] P. Wei, W. Yuan, F.F. Xue, W. Zhou, R.H. Li, D.T. Zhang, T. Yi, Deformylation reaction-based probe for in vivo imaging of HOCl, Chem. Sci. 9 (2018) 495–501.
[25] Y. Yang, F. Huo, C. Yin, M. Xu, Y. Hu, J. Chao, Y. Zhang, T.E. Glass, J. Yoon, A novel method for the synthesis of 1,2-benzisoxazoline-3-one and its application to hypochlorite recognition, J. Mater. Chem. B 4 (2016) 5101–5104.
[26] B.C. Zhu, P. Li, W. Shu, X. Wang, C.Y. Liu, Y. Wang, Z.K. Wang, Y.W. Wang, B. Tang, Highly specific and ultrasensitive two-photon fluorescence imaging of native HOCl in lysosomes and tissues based on thiocarbamate derivatives, Anal. Chem. 88 (2016) 12532–12538.
[27] B.B. Deng, M.G. Ren, X.Q. Kong, K. Zhou, W.Y. Lin, Development of an enhanced turn-on fluorescent HOCl probe with a large Stokes shift and its use for imaging HOCl in cells and zebrafish, Sens. Actuators, B 255 (2018) 963–969.
[28] J. Lv, F. Wang, T. Wei, X. Chen, Highly sensitive and selective fluorescent probes for the detection of HOCl/OCl^- based on fluorescein derivates, Ind. Eng. Chem. Res. 56 (2017) 3757–3764.
[29] J.J. Hu, N.K. Wong, M.Y. Lu, X.M. Chen, S. Ye, A.Q. Zhao, P. Gao, R.Y. Kao, J.G. Shen, D. Yang, HKOCl-3: a fluorescent hypochlorous acid probe for live-cell and in vivo imaging and quantitative application in flow cytometry and a 96-well microplate assay, Chem. Sci. 7 (2016) 2094–2099.
[30] Y.-R. Zhang, Y. Liu, X. Feng, B.-X. Zhao, Recent progress in the development of fluorescent probes for the detection of hypochlorous acid, Sens. Actuators, B 240 (2017) 18–36.
[31] Y.W. Jun, S. Sarkar, S. Singha, Y.J. Reo, H.R. Kim, J.J. Kim, Y.T. Chang, K.H. Ahn, A two-photon fluorescent probe for ratiometric imaging of endogenous hypochlorous acid in live cells and tissues, Chem. Commun. 53 (2017) 10800–10803.
[32] B. Zhu, L. Wu, H. Zhu, Z. Wang, Q. Duan, Z. Fang, P. Jia, Z. Li, C. Liu, A highly specific and ultrasensitive two-photon fluorescent probe for imaging native hypochlorous acid in living cells, Sens. Actuators, B 269 (2018) 1–7.
[33] P. Chen, Z. Zheng, Y. Zhu, Y. Dong, F. Wang, G. Liang, A bioluminescent turn-on probe for sensing hypochlorite in vitro and in tumors, Anal. Chem. 89 (2017) 5693–5696.
[34] Q.A. Best, N. Sattenapally, D.J. Dyer, C.N. Scott, M.E. McCarroll, pH-dependent Si-fluorescein hypochlorous acid fluorescent probe: spirocycle ring-opening and excess hypochlorous acid-induced chlorination, J. Am. Chem. Soc. 135 (2013) 13365–13370.
[35] J.J. Hu, N.K. Wong, Q.S. Gu, X.Y. Bai, S. Ye, D. Yang, HKOCl-2 series of green BODIPY-based fluorescent probes for hypochlorous acid detection and imaging in live cells, Org. Lett. 16 (2014) 3544–3547.
[36] M.G. Ren, B.B. Deng, K. Zhou, X.Q. Kong, J.Y. Wang, G.P. Xu, W.Y. Lin, A lysosome-targeted and ratiometric fluorescent probe for imaging exogenous and endogenous hypochlorous acid in living cells, J. Mater. Chem. B 4 (2016) 4739–4745.
[37] X.B. Dong, G.X. Zhang, J.B. Shi, Y.C. Wang, M. Wang, Q. Peng, D.Q. Zhang, A highly selective fluorescence turn-on detection of ClO^- with 1-methyl-1,2-dihydropyridine-2-thione unit modified tetraphenylethylene, Chem. Commun. 53 (2017) 11654–11657.
[38] Y.R. Zhang, Z.M. Zhao, J.Y. Miao, B.X. Zhao, A ratiometric fluorescence probe based on a novel FRET platform for imaging endogenous HOCl in the living cells, Sens. Actuators, B 229 (2016) 408–413.
[39] Q.L. Xu, K.A. Lee, S.Y. Lee, K.M. Lee, W.J. Lee, J. Yoon, A highly specific fluorescent probe for hypochlorous acid and its application in imaging microbe-induced HOCl production, J. Am. Chem. Soc. 135 (2013) 9944–9949.
[40] Z.N. Sun, F.Q. Liu, Y. Chen, P.K.H. Tam, D. Yang, A highly specific BODIPY-based fluorescent probe for the detection of hypochlorous acid, Org. Lett. 10 (2008) 2171–2174.
[41] S.L. Shen, X.Q. Huang, Y.Y. Zhang, Y. Zhu, C. Hou, Y.Q. Ge, X.Q. Cao, Ratiometric fluorescent probe for the detection of HOCl in lysosomes based on FRET strategy, Sens. Actuators, B 263 (2018) 252–257.
[42] C.Y. Zhang, Q.C. Nie, I. Ismail, Z. Xi, L. Yi, A highly sensitive and selective fluorescent probe for fast sensing of endogenous HClO in living cells, Chem. Commun. 54 (2018) 3835–3839.
[43] J. Kang, F. Huo, Y. Zhang, J. Chao, R.M. Strongin, C. Yin, Detecting intracellular ClO^- with ratiometric fluorescent signal and its application in vivo, Sens. Actuators, B 273 (2018) 1532–1538.
[44] H. Zhang, F. Huo, Y. Zhang, C. Yin, Mono-or di-naphthalimides as fluorophore to detect hypochlorous acid (HOCl) by ratiometric fluorescent signal and their biological application, Sens. Actuators, B 269 (2018) 180–188.
[45] B.C. Zhu, C.C. Gao, Y.Z. Zhao, C.Y. Liu, Y.M. Li, Q. Wei, Z.M. Ma, B. Du, X.L. Zhang, A 4-hydroxynaphthalimide-derived ratiometric fluorescent chemodosimeter for imaging palladium in living cells, Chem. Commun. 47 (2011) 8656–8658.
[46] B.C. Zhu, Z.K. Wang, Z.Y. Zhao, W. Shu, M. Zhang, L. Wu, C.Y. Liu, Q.X. Duan, P. Jia, A simple highly selective and sensitive hydroquinone-based two-photon fluorescent probe for imaging peroxynitrite in live cells, Sens. Actuators, B 262 (2018) 380–385.
[47] Z. Wang, Z. Geng, Z. Zhao, W. Sheng, C. Liu, X. Lv, Q. He, B. Zhu, A highly specific and sensitive ratiometric fluorescent probe for carbon monoxide and its bioimaging applications, New J. Chem. 42 (2018) 14417–14423.
[48] S. Xu, H.W. Liu, X.X. Hu, S.Y. Huan, J. Zhang, Y.C. Liu, L. Yuan, F.L. Qu, X.B. Zhang, W. Tan, Visualization of endoplasmic reticulum aminopeptidase 1 under different redox conditions with a two-photon fluorescent probe, Anal. Chem. 89 (2017) 7641–7648.
[49] H. Zhu, J.L. Fan, J.Y. Wang, H.Y. Mu, X.J. Peng, An "enhanced PET"-based fluorescent probe with ultrasensitivity for imaging basal and elesclomol-induced HClO in cancer cells, J. Am. Chem. Soc. 136 (2014) 12820–12823.
[50] K. Setsukinai, Y. Urano, K. Kakinuma, H.J. Majima, T. Nagano, Development of novel fluorescence probes that can reliably detect reactive oxygen species and distinguish specific species, J. Biol. Chem. 278 (2003) 3170–3175.
[51] Y. Koide, Y. Urano, S. Kenmoku, H. Kojima, T. Nagano, Design and synthesis of fluorescent probes for selective detection of highly reactive oxygen species in mitochondria of living cells, J. Am. Chem. Soc. 129 (2007) 10324–10325.
[52] Y.X. Liao, M.D. Wang, K. Li, Z.X. Yang, J.T. Hou, M.Y. Wu, Y.H. Liu, X.Q. Yu, A highly sensitive and selective "turn-on" fluorescent probe for hypochlorous acid monitoring, RSC Adv. 5 (2015) 18275–18278.
[53] T. Guo, L. Cui, J.N. Shen, R. Wang, W.P. Zhu, Y.F. Xu, X.H. Qian, A dual-emission and large Stokes shift fluorescence probe for real-time discrimination of ROS/RNS and imaging in live cells, Chem. Commun. 49 (2013) 1862–1864.