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Mini Review

Recent Advances in Quinoline Based Fluorescent Probes for Bio-imaging Applications

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Abstract

Bioimaging has emerged as a prominent non-invasive technique for early diagnosis of several diseases especially cancer and neurodegenerative diseases. A lot of efforts have been devoted for the development of appropriate fluorescent probes which have great utility for experiments including cellular staining, tracking biomolecules of interest and, detection of specific bioanalytic in the cellular organisms. Quinoline-based scaffolds are among one of the widely explored moieties as molecular probes and chemosensory due to their interesting biological, photophysical and pharmacological properties. Herein, we have discussed some quinolone based fluorescent probes for bio-imaging applications.

Keywords: Quinoline; Fluorescent probes; Bio-imaging

Abbreviations: MPF: Multiphoton Fluorescent; 3PA: Three Photon Absorption; ICT: Intramolecular Charge Transfer; ESIPT: Excited State Intramolecular Proton Transfer; FRET: Forster Resonance Energy Transfer; PET: Photo-Induced Electron Transfer; CHEF: Chelation Enhanced Fluorescence; ROS: Reactive Oxygen Species

Introduction

Fluorescence imaging is a growing interest of field due to low cost, easy handling, high sensitivity, specificity, and target orientation [1,2]. It is an advanced non-invasive imaging technique that can detect, visualize, and characterize morphological and dynamic phenomena of biology at the molecular level in multi-dimensional fashions. Several fluorescent probes have slowly and steadily evolved and are now indispensable imaging tools in the field of molecular biology and medicine [3,4]. Among them quinoline-based fluorescent probes have been extensively explored due to their interesting biological, photophysical and pharmacological properties. In this mini review, we aim to summarize recent developments in quinoline-based fluorescent probes for bioimaging applications.

Quinoline-based scaffolds and their bioimaging application

Quinoline consists of benzene ring fused with a pyridine moiety, also known as 1-azanapthalene and benzo[b]pyridine [5]. It belongs to a privileged class of heterocyclic aromatic compound and exhibits a broad range of biological and pharmaceutical activities such as antibacterial, antioxidant, anticancer, anti-inflammatory, antimalarial, and antifungal [6-10]. In addition, it possess interesting fluorescence properties, which has been utilized in the development of various quinoline appended fluorescent molecules and has been exploited in the field of bio-imaging as molecular probes/chemo-sensors for monitoring the interactions with target molecules through the changes in fluorescence emission/intensity [11-19].

In 2020, Tian et al. [13] synthesized a series of quinoline based multiphoton fluorescent probe (MPF) for selective detection of lipid droplets in live cells. This MPF probe 1 exhibited ICT effect, deeper tissue penetration, lower autofluorescence and lower photo-toxicity (Figure 1). The three-photon absorption, 3PA cross sections of 1 was significantly enhanced when it binds to liposome and on the other hand due to large stokes Shift, it was highly selective to

lipid droplets in living cells [13]. For detection and imaging of Aβ aggregates in Alzheimer's disease, Yi et al. reported a water soluble two quinoline-malononitrile-based NIR fluorescent probes 2 and 3. These NIR probes were demonstrated for imaging of Aβ aggregates in *in-vitro* and in brain sections from triple transgenic mice of AD [14]. A turn-on quinoline and benzothiazole based chemo-sensor 4 was developed for the detection of Hg^{2+} through ESIPT mechanism. This chemo-sensor was successfully applied for the detection of Hg^{2+} in HeLa cells. Song et al. [16] reported quinoline containing two-input fluorescent probe (5, QME-N3) with two distinct reactive sites, the α, β-unsaturated carbonyl at 2-site and 6-azido group, which were specific acceptors of RSH and H_2S respectively in live cells [16]. Chenoweth and his group rationally designed and synthesized a series of highly tunable quinoline-based small fluorescent molecule 6 and explored for various applications such as tunable photophysical properties and live-cell imaging followed by fluorescence response to intracellular pH [17]. During cellular diffusion-controlled processes, intracellular viscosity participates in the transportation and interaction of biomolecules and also abnormalities in viscosity produces many dysfunctions, such as Alzheimer's disease and atherosclerosis [18] (Figure 2).

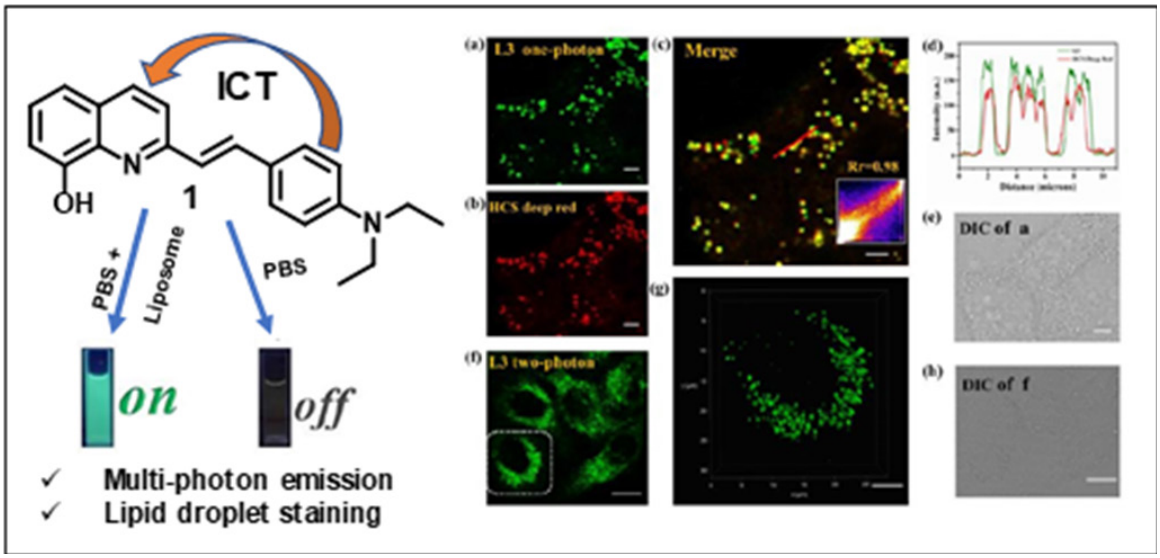

Figure 1: Structure of ICT based fluorescent probe 1 and Confocal images of live HeLa cells.

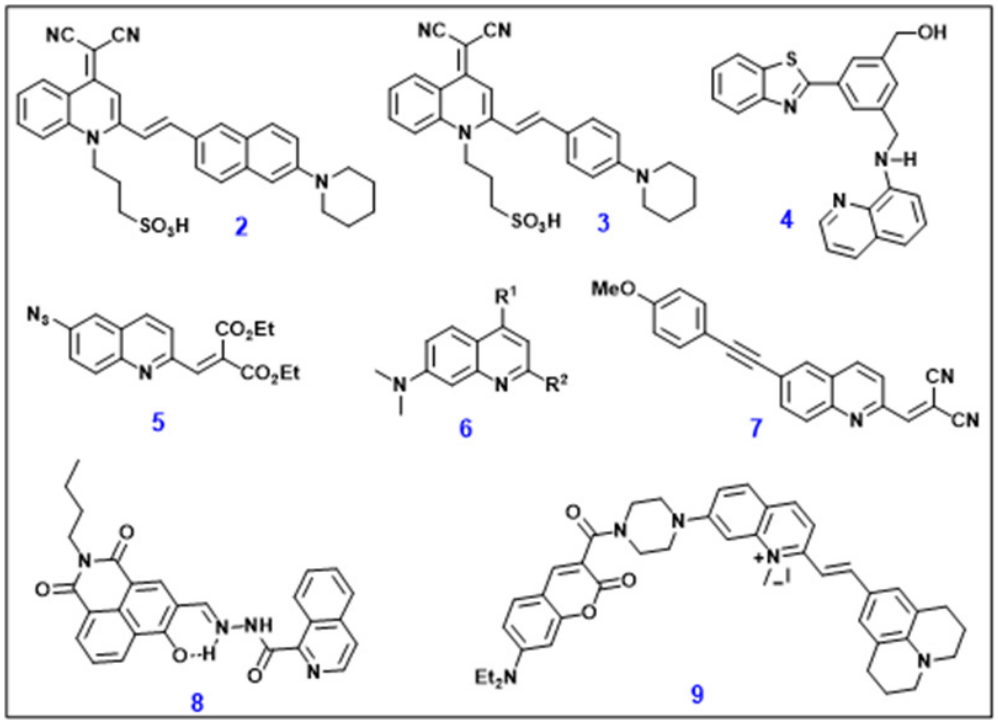

Figure 2: Structure of quinoline based fluorescent molecules for bio-imaging.

To visualize viscosity, Meng et al. [18] developed a two-photon fluorescent probe 7 which displayed off-on response with the increase of viscosity and also demonstrated imaging of intracellular viscosity in HeLa cells and zebrafish. In 2022, Xu et al. [19] discovered a reversible "turn-on" fluorescent probe 8 (NIQ) based on naphthalimide appended isoquinoline Schiff base for the detection of Al^{3+} in living cells. The sensing process involves inhibition of photo-induced electron transfer (PET) and the chelation-enhanced fluorescence (CHEF) process [20]. Sulfur dioxide (SO_2) displayed important role in the regulation of insulin levels in the blood and lower blood pressure, but an elevated level also causes several diseases such as diarrhea, low blood pressure and cancer, neurological disease and cardiovascular disease. In order to detect endogenous and exogenous HSO_3^-/SO_3^{2-} in live cells, recently Liu and his group synthesized near-infrared FRET fluorescent probe 9 which consisted of coumarin-quinoline-julolidine skeleton. This probe showed potential for differentiating normal cells from cancer cells and also targeting lysosomes [21].

Conclusion

This review discusses some recently developed quinoline-based fluorescent probes and highlights their potential use in cellular systems as imaging agents targeting liposomes, lysosomes, Aβ aggregates, intracellular pH and viscosity. Further, quinoline-based chemo-sensors for detection of toxic metal ions such as Hg^{2+} and Al^{3+} and reactive oxygen species (ROS) like RSH, H2S and HSO_3^-/SO_3^{2-} have also been designed and developed successfully. These probes showed advantages of a wide linear range, high quantum yields and low detection limit. Thus, these probes can help in early diagnosis of diseases like cardiovascular, cancer, atherosclerosis and neurodegenerative diseases, thereby forming the basis of most medical decision-making and limiting healthcare costs.

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