

Figure 16. The HCDs with different substituents at the middle position

Compared with that of the parent molecule, the absorption spectrum of this molecule has a blue shift of about 60-80 nm, with a small shoulder peak at 500-600 nm, and a significant improvement of photostability and fluorescence quantum yield. In addition, Chen et al. [73] derived a H₂S fluorescence-enhanced fluorescent probe from 19e (19f).

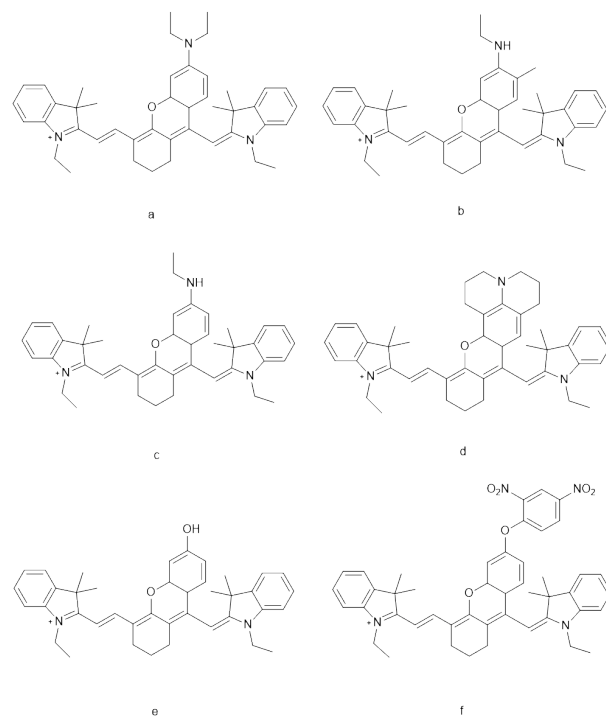


Figure 19. The HCDs with the structure "xanthene-cyanine"

Since the middle position substitution has a major impact on HCD molecules, and plays an important role in expanding molecular applications, the derivatization of dye molecules by middle position substitution can realize the fluorescence detection for small molecules and ions like hypochlorous acid, palladium, and promote the application of the HCDs in biological analysis. Liu et al. research team [77] introduced an acyl group to the middle carbonyl of the polymethine chain, and managed to determine the mitophagy in biological cells. Zhao et al. [78] introduced tetraphenylene at the middle position of heptamethine indocyanine, which successfully transforms heptamethine molecules as photothermal conversion materials in cancer treatment, for the introduction effectively avoids the aggregated fluorescence quenching of dye molecules, and improves the photothermal conversion efficiency.

4. CONJUNCTION OF THE HCDS WITH FUNCTIONAL MATERIALS

The application of the HCDs is limited by their water solubility, photostability, and fluorescence quantum yield. To expand the application scope, it is necessary to improve the aggregation degree, fluorescence properties and photostability by combining the HCDs with functional materials (such as metal oxide sols, polymers, surfactants, etc.).

Zheng et al. research team [79] combined cyanine dyes with metal oxides (TiO₂, and SiO₂) or cetrimonium bromide

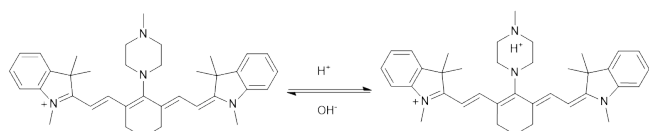


Figure 17. The HCDs as pH sensor

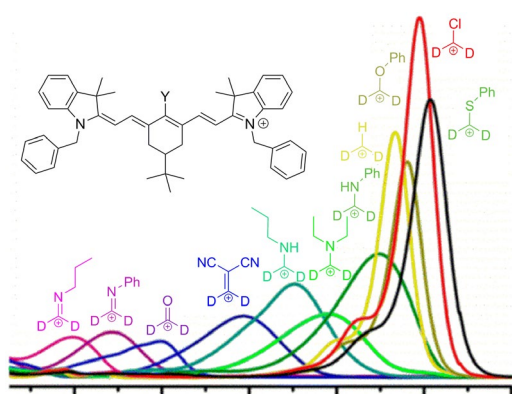


Figure 18. Relationship of middle position substituents with absorption spectra of the HCDs [72]

The middle position substituents not only directly affect the properties of HCD molecules, but also regulate their photostability and fluorescence properties by combining with the conjugated chains. Chen et al. [73] used phenolic hydroxyl to replace the middle position chlorine of heptamethine indocyanine, and obtained several fluorescent probes of the structure "xanthene-cyanine" (Figure 19a-e).

(CTAB), and observed a large increase in the photostability of the dyes, as well as an increment of the pH response range, compared with the pure dye solutions. Their research sheds new light on how to expand the use scope and application of the dyes.

The HCDs are also complexed with polyethylene glycol (PEG) to increase their water solubility, and then applied to the photodynamic therapy of cancer cells [80, 81]. Pais-Silva et al. [82] loaded IR780 into PEG-succinate vitamin E micelles, which increases its solubility in water by nearly 10 times, reduces its aggregation in aqueous solution, and greatly lowers the clinical dose for cancer cell removal. Zhang et al. [83] and St-Lorenz et al. [84] loaded the HCDs onto nanoparticles like SiO₂, and PEG-polycaprolactone (PCL), and observed marked improvements to dispersibility, photostability and photothermal conversion efficiency. The combined materials can be used clinically as photothermal conversion materials in cancer therapy.

5. CONCLUSIONS

Since the approval of the ICG by the FDA, more and more researchers turned their attention to the application of the HCDs in biological analysis. There is ample room to improve the HCD performance, owing to their defects in water solubility, photostability, and fluorescence quantum yield, as well as the many modifiable sites. In the field of biological analysis, several HCDs with excellent performance have been developed for biological imaging, photothermal conversion, and photoacoustic conversion, thanks to the HCDs' low biological toxicity, lack of obvious side effects, and good targeting and clearing ability of cancer cells. In addition, the HCDs have been applied to photoelectric conversion tasks (e.g., Dye-Sensitized Solar Cells), because their wavelength is adjustable.

The further research on the structural modification of the HCDs will surely make up for their structural defects, and the modified HCDs will achieve better application results in biological analysis, photoelectric conversion, and other fields.

ACKNOWLEDGMENT

This work is funded by the Youth Science Fund, Northeast Petroleum University, Fundamental Research Funds for Undergraduate Universities in Heilongjiang Province, under the project "Fluorescence probes based on heptamethine indocyanine and their application in metal ion detection" (Grant No.: 2018QNNQ-03).

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