A Review of Fluorescein Based detection probes for Hg^{2+}, Cu^{2+} and Zn^{2+} in Water

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Abstract

Water is the cheapest renewable energy source available on earth without any negative effects. However, the present human activities and the natural catastrophes are making it more vulnerable to negative effects by the release of heavy metals in the natural water resources. These heavy metal ions in water forms free radicals and cause high health concerns.Hence,in present scenario critical issue is fast and preciseddetection of heavy metal ions. Detection of these heavy metal ions through fluorometric techniques has emerged out as an important class in the area of heavy metal detection. Out of the small fluorescent molecules used for detecting these heavy metal ions, Fluorescein based derivatives are widely encountered. Fluorescein derivatives have good solubility in water and alcohol therefore are successfully used to detect various heavy metal ions such Pd2+, Hg2+, Zn2+, Pb2+ etc. In this review, we have summarized the various fluorescein based fluorescent probes for detecting Hg^{2+}, Cu^{2+} and Zn^{2+} in the last few years.

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Introduction

The term renewable means inexhaustible or sustainable, so the renewable energy resources are the one that are clean, easily available and are inexhaustible and their present demand won't lead to their shortage in future. Out of the available renewable energy sources, Water is the one that has no negative effects and is the cheapest. However, with the advancement of technology, due to human activities and natural calamities the water resources are getting more prone to heavy metal pollution. Heavy metals are the components that have low density[1a], and as they are non-biodegradable they have ill effects on human health[1b,1c,1d,1e]. Due to their accumulation in biosphere they enter in food chain and finally in living beings resulting in ill effects on human health[1f,1g]. Heavy metal pollution is of high concern, not only among the community with scientific background, but also general public, which is aware of the ill-effects of these heavy metal ions are highly concerned. Even that is the fact that living system has need of some heavy metals, but there toxicity makes them capable of causing serious environmental problems and health issues[1h]. Some heavy metal ions, such as Fe(III), Zn(II), Cu(II), Co(II), Mn(II), and Mo(VI), are required for the maintenance of human metabolism. However, concentrations above permissible limits of these heavy metal ions can cause many adverse health effects[1h,1i]. However, Hg(II), Cd(II), Pb(II), and As(III) are the heavy metal ions, whose even the little concentration can cause severely bad effects on human beings. Accumulation of these with time in the bodies of humans and animals can cause severe side effects[1i]. In the present review, we have tried to sum up Hg^{2+}, Cu^{2+} and Zn^{2+} sensors discovered in last few years.

Hg^{2+} sensors

Mercury being very toxic, in living cells is a major health concern as it is the major cause of damaging of central nervous system and leads to cognitive and Minamata diseases[1j,2].That is why it is necessary to find out some efficient method to detect it selectively and sensitively as well. For this purpose,fluorescence based methods are found to be more attractive and efficient. Fluorescein receptors have been proposed because of its long emission and absorption wavelengths, large absorption coefficient, excellent photo physical properties, good quantum yield and good photo-stability [3].

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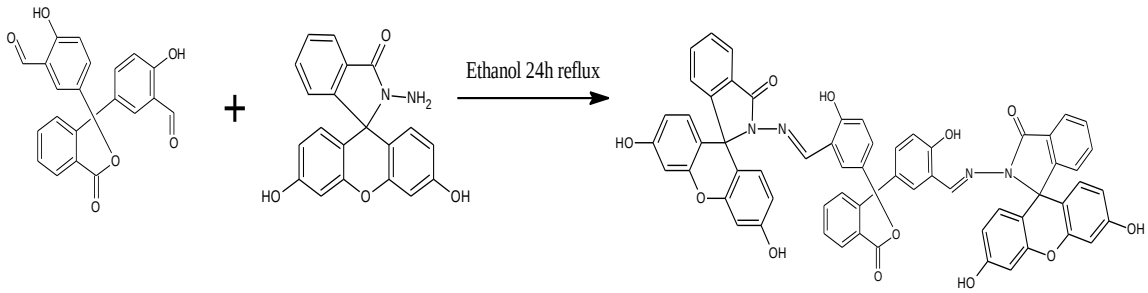
Erdemir et al. [6] synthesized a phenolphthalein fluorescein dye derivative(PF) that shows selectivity and sensitivity towards both Zn^{2+} and Hg^{2+} ion and act as a dual responding probe in EtOH-H_2O much effectively. Fluorescence emission in presence of Zn^{2+} and Hg^{2+} are observed at 500 & 600nm. The detection limit by PF for Zn^{2+}microM and $Hg^{2+}$is 1.16 microM. Here a probe based on fluorescein is synthesized that can show double metal detection within various binding modes. [4] The synthesis of PF given (as scheme 1) where di-aldehyde based phenolphthalein derivative was being prepared by hexamethyletetraamine in TFA[4] and Fluorescein hydrazine was being prepared by Fluorescein and hydrazine monohydrate in methanol[5].

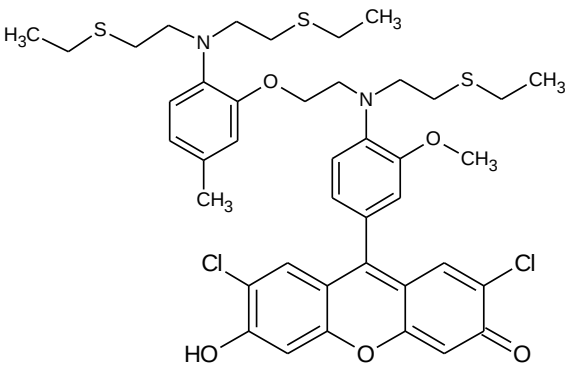
SCHEME1:



[PF]

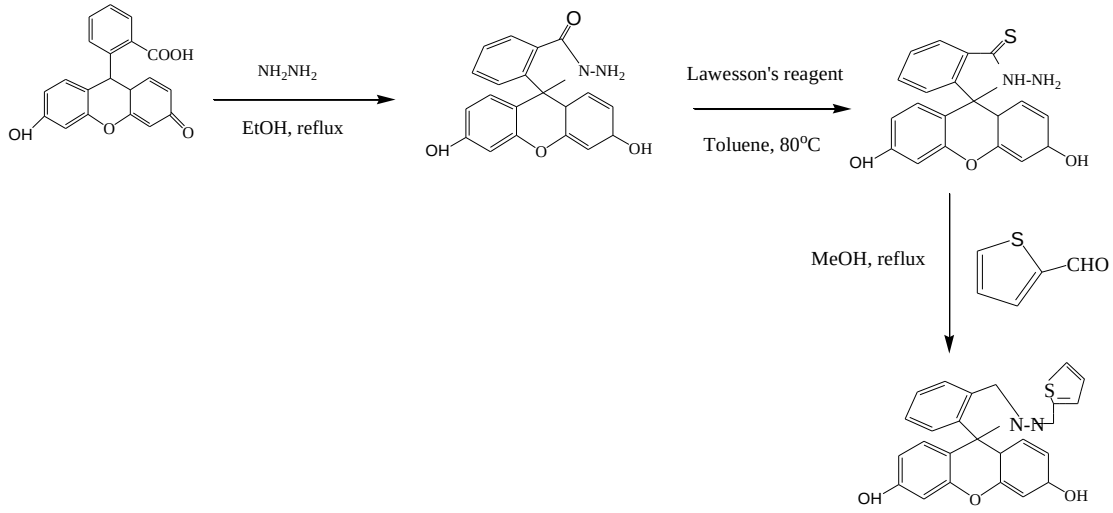
Lin et al. designed highly selective and sensitive fluorescent Hg^{2+} sensor i.e. based on PET, with N-Ethyl thioethyl-N-[N'N'-(2'-Diethyl thio-ethylamino)-5'-methyl-phenoxy-ethyl]-2-methoxy aniline. The probe senses Hg^{2+} in living cell along with an emission band of fluorescein at 529nm and the addition of Hg^{2+} to solution of the formed sensor of Hg^{2+} gives emission maximum at 539nm and therefore this probe (scheme 2) is applied to image Hg^{2+} living cells and is highly efficient fluorescent sensor for Hg^{2+} in aqueous solution[7].

SCHEME 2:



Feng et al. designed a fluorescent probe FLS2 which is actually soluble in water and is based on thio-oxofluoresceinderivative. The probe FLS2 is a colorimetric and ratiometric fluorescent probe which have been proven by UV-Vis absorption and Fluorescent spectra studies and obviously the probe exhibits high sensitivity and selectivity to Hg^{2+}. FLS2 probe can also be used as an indicator for Hg^{2+} with reversible response and the detection limit for this is 39nM. The sensor being much excellent bio compatible& low cytotoxic as well can beefficiently isused for imaging or monitoring Hg^{2+} in living cells[8].

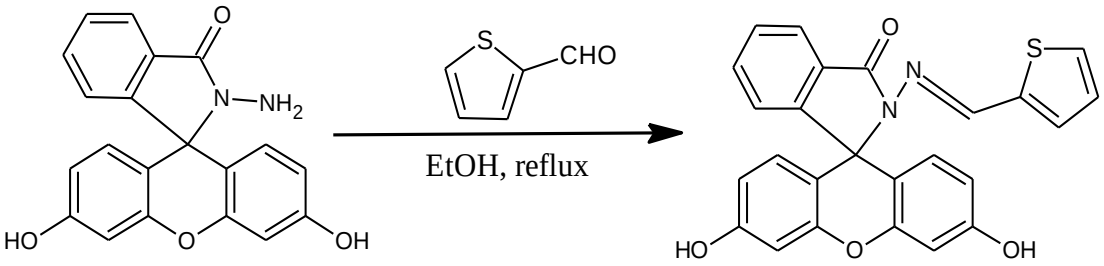
SCHEME 3:



Chiou et al. synthesized fluorescent receptor that is thiophene appended fluorescein hydrazone derivative (FT) using 2-thiophene carboxaldehyde which gives colorimetric change when Hg^{2+} is bound in DMSO/H_2O (1:9) and the color change observed is orange from colorless. Receptor FT used to show major absorption spectra at 348nm and when bind to Hg^{2+} gives the same

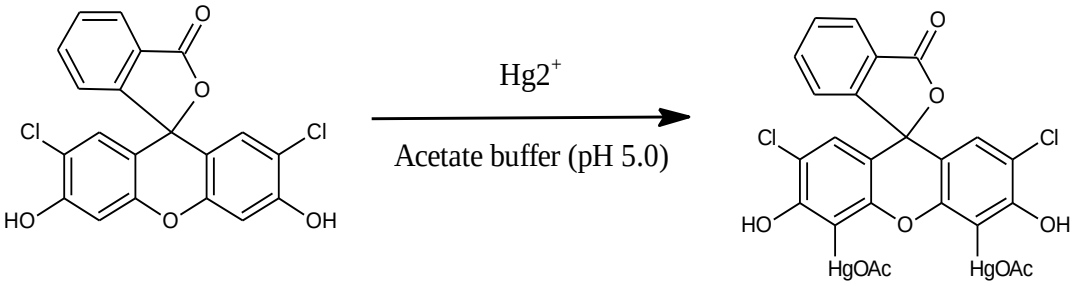
spectra at 502nm in DMSO/H_2O(1:9) and FT's detection limit towards Hg^{2+} is about 0.24ppm. The FT is synthesized as in the following scheme[9]:

SCHEME 4:



Chang et al. synthesized chemo-dosimetric signaling system for determination of Hg^{2+} ions in aqueous medium, selectively and is based on a readily available dichlorofluorescein. It exhibit absorption band at 475nm shoulder peak and 505nm of maximum absorption wavelength in acetate-buffered aqueous solution with 10% DMSO and then decreased gradually decreased to 483 and 533nm when treated with Hg^{2+}. On treatment with Hg^{2+} ion, emission band around 528nm get quenched. Signaling is being caused by the mercuration at 4,5-positions of xanthene ring and the detection limit for the probes is $7.5x10^{-6}$ M and this is how Hg^{2+} is being sensed easily.[10]

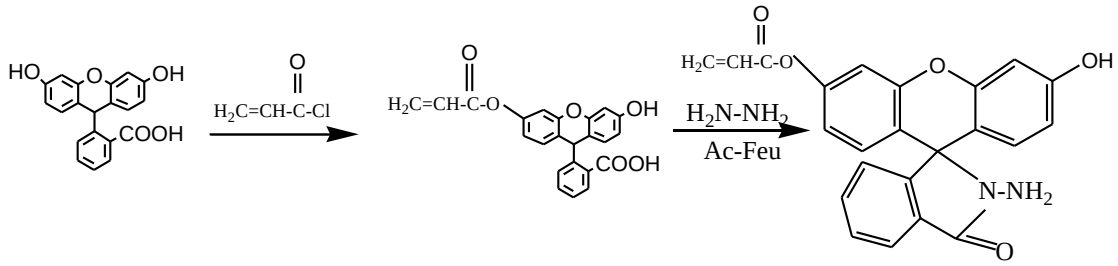
SCHEME 5:



Guang et al. designed acryloyl fluorescein hydrazine(ACFH) to improve water solubility of various materials that generally senses heavy metals. Firstly, propylene acyl fluorescein(AC-Flu) was synthesized using acryloyol chloride and then using AC-Flu, ACFH was being synthesized using hydrazine hydrate. ACFM in the presence of Hg^{2+} shows fluorescence – enhancement performance (at 512nm) which can be observed with naked eyes. Two absorption

peaks at 275nm and 290nm were observed by UV-Vis spectra and after the addition of Hg^{2+}, one peak at 445nm was being observed. Moreover, its detection limit towards Hg^{2+} is about $0.86x10^{-9}$ $molL^{-1}$ and the co-ordination constant is $3.36x10^{9}$. Here, ACFM possess great potential application in Hg2+ detection in various water environments and its synthesis is as follows[11].

SCHEME 6:

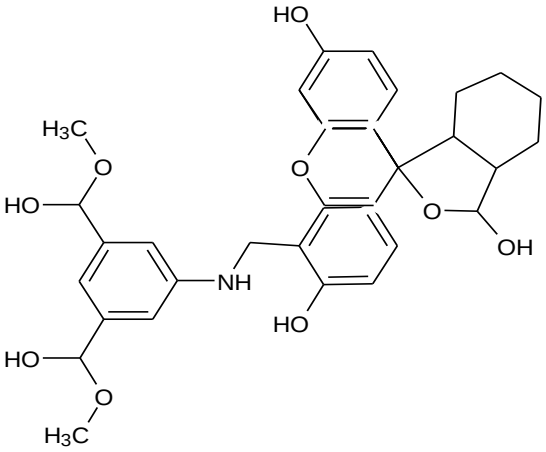


Cu(II) Sensors:

Copper is one of the most important heavy metals and is very useful in living systems as well. It is generally considered to be a trace element as it is essential in trace amounts and when taken in excess amount causes unexpectedly dangerous harms including Wilson disease and Alzheimer's disease and many more. And thus fluorescent based probes for sensing heavy metal ions are found to be the accurate method for monitoring or imaging this metal ion in living systems as well.

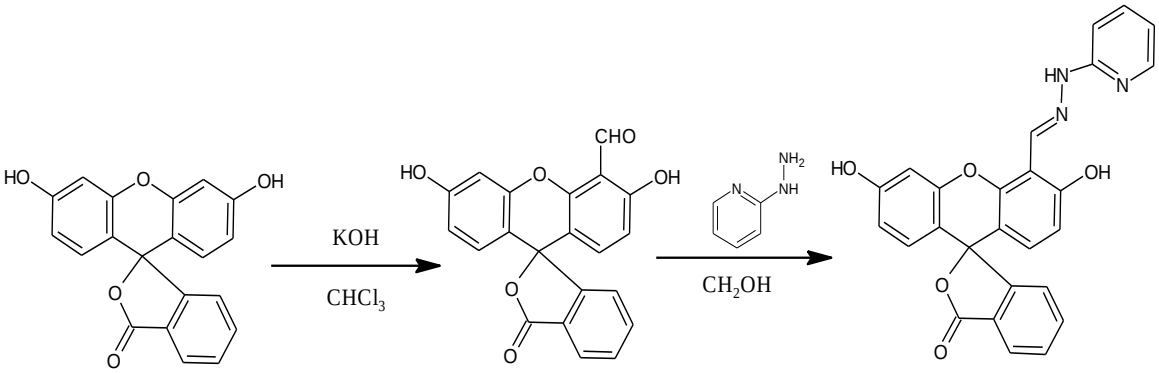
Jiao et al. designed sensor FR-L for detection of Cu(II) ions in living system. The probe involving 5-aminoisophthalic acid methyl ester with fluorescein was synthesized & were characterized by ESI-MS,^{1}H-NMR etc. Analysis with addition of Cu(II) ions, sensor shows quenching. Sensor selectively detects Cu(II) and changes in absorption were found. FR-L was prepared by Schiff Base reactions of FR-I and 5-aminoisophthalic acid methyl ester in ethanol solution that showed high selctivity towards Cu^{2+} ions. The same probe was studied fo detection of Cu^{2+} ion in living cells[12].

SCHEME 7:



Hou et al. designed fluorescein based probe (H_2L) for double detection of Al^{3+} and Cu^{2+}. H_2L gives high selectivity towards two different ions along with their different fluorescence signals & different binding modes as well in different media. H_2L give high selectivity when binds Al^{3+} to form complex and thus it gives pale pinkto orange yellow change in colour& a fluorescene enhancement at 520nm. The detection limit is $7.32x10^{-8}$M &$1.47X10^{-8}$M towards Al^{3+} and Cu^{2+} respectively.[13]

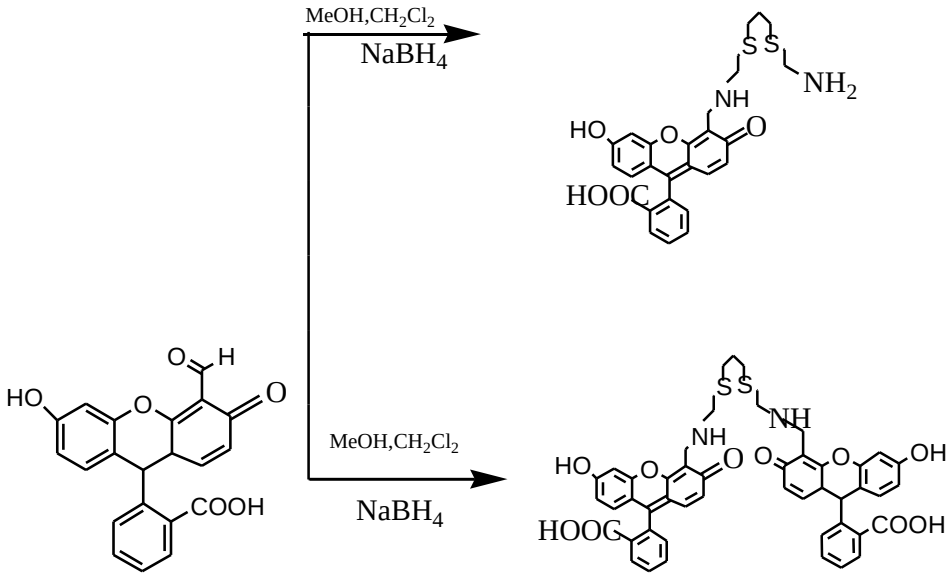
SCHEME 8:



Tachapermpon et al. designed two fluoro-ionphores by covalently appending fluorescein moieties to sulphide containing ligands,MF3 and DF3 both the synthetic sensors were developed to give highly selective and sensitive responses towards Cu^{2+}in aqueous media. They were simply designed by Reiman-Tieman reaction, imine formation and reduction as well. The detection limits of MF3 and DF3 towards Cu^{2+} are 0.23 and 0.43 ppb respectively. The sensors show chromogenic cleavage and are ‘’visual eye’’ indicators and shows color

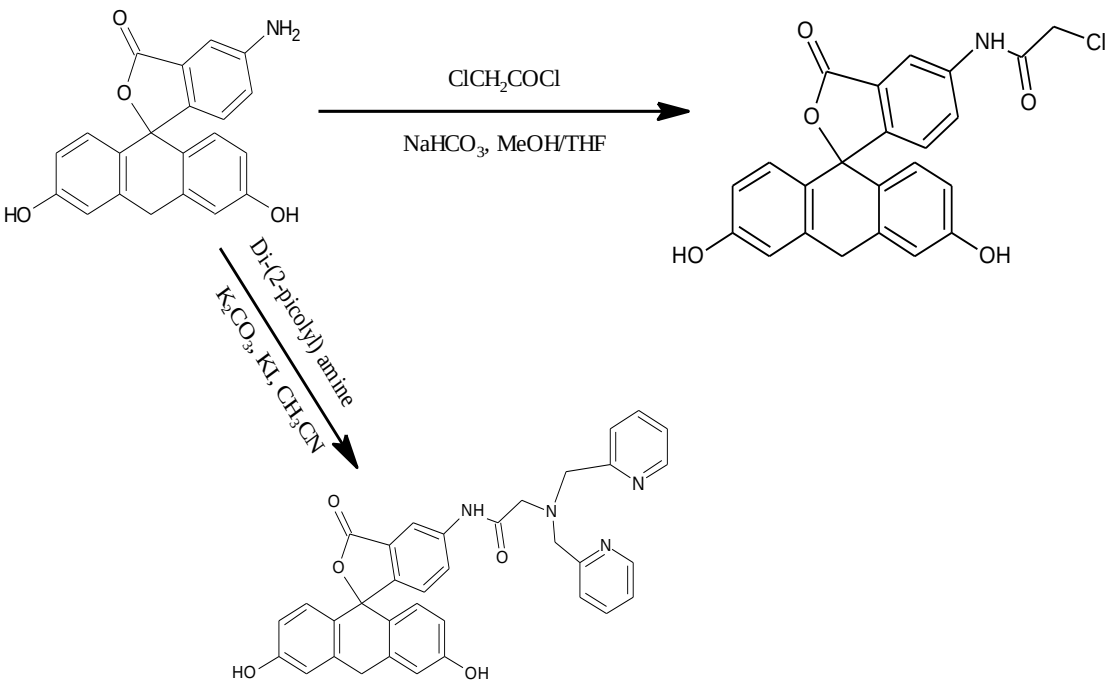
change from yellow to orange. Sensor is also being used for imaging and monitoring of HepG-2 cellular system.[14]

SCHEME 9:



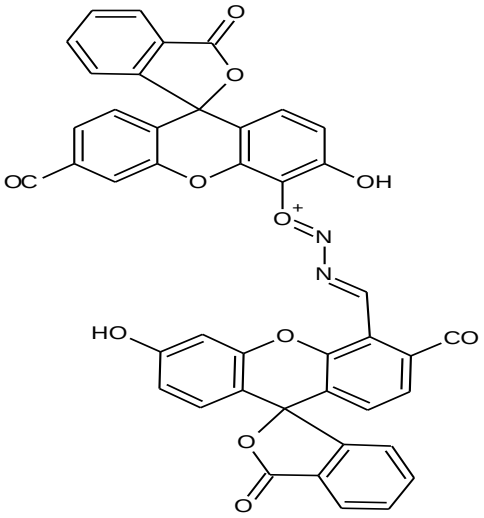
Choi et al. synthesized a sulphide-selective chemo-signaling system which was based on Cu^{2+} complex of fluorescein derivative consisting of a diphenyl amine binding site along with it. In the presence of Cu^{2+} ion, the probe (fluorescein DPA conjugate) exhibits a selective turn-on type signalingbehavior. And the detection limit for the synthesized molecule towards Cu^{2+} in 420nm in 100% aqueous method. DPA moiety is being used for formation of many supra molecular systems which acts as a good metal sensors and the compound give selective off-on type response towards sulphideions in aqueous media[15].

SCHEME 10:



Rathod et al. synthesized a flourometric chemosensor,1,4-bis(1-fluorescem)-2,3-diaza-1,3-butadiene that shows efficient binding for Cu^{2+} in H_2o and gives a naked eye result.The characteristics changes in UV-Vis absorption to longerwavelength by 130 nm is being observed with a naked-eye rapid change in color to deep yellow from colorless and get quenched with a maxima at 519nm. In 1% DMSO-tris buffer solution.Its detection limit towards Cu^{2+} in acetonitrile is 20microM in UV-spectroscopy and on the other hand in aqueous solution, the limit is 1.25microM in fluorescence spectroscopy. Detection of Cu^{2+} in aqueous media is necessary as it is highly toxic at high concentration and is involved in diseases like Alzheimer's and Parkinson's etc. [16].

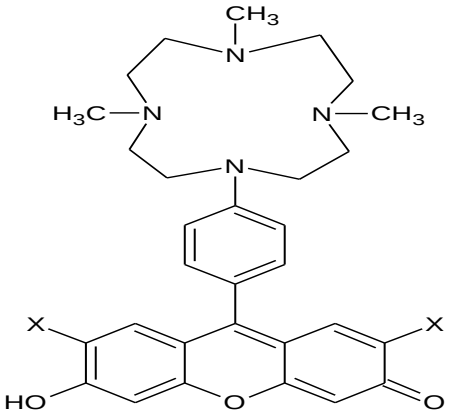
SCHEME 11:



Zn^{2+} sensors:

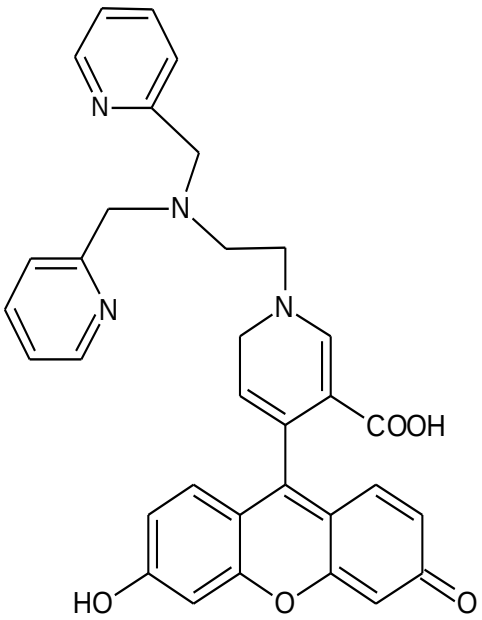
Zinc, the second most abundant element in human body behind iron plays an important role in many cellular processes and in bioinorganic chemistry as well. Zn^{2+} at the most gets tightly bound in proteins and has ability to modulate various channels of ions and causes neuronal death, neurodegenerative disorders and many more. Due to these diverse functions, sensing or imaging of Zn^{2+} by fluorescent-based probes accurately is much important task to do. Nagano et al. developed fluorescent probes for the detection of Zn^{2+} by bounding the macrocyclic polyzmine as such to fluorescein. In this, fluorescence is being quenched due to PET as amino group is attached of phthalic ring of fluorescein ,moreover nitrogen of fluorophore aniline result in lowered pK_a values. The detection limit of probe is 500nM for both under pH 7.5[17].

SCHEME 12: turn-on type fluorescent probe of Zn^{2+}



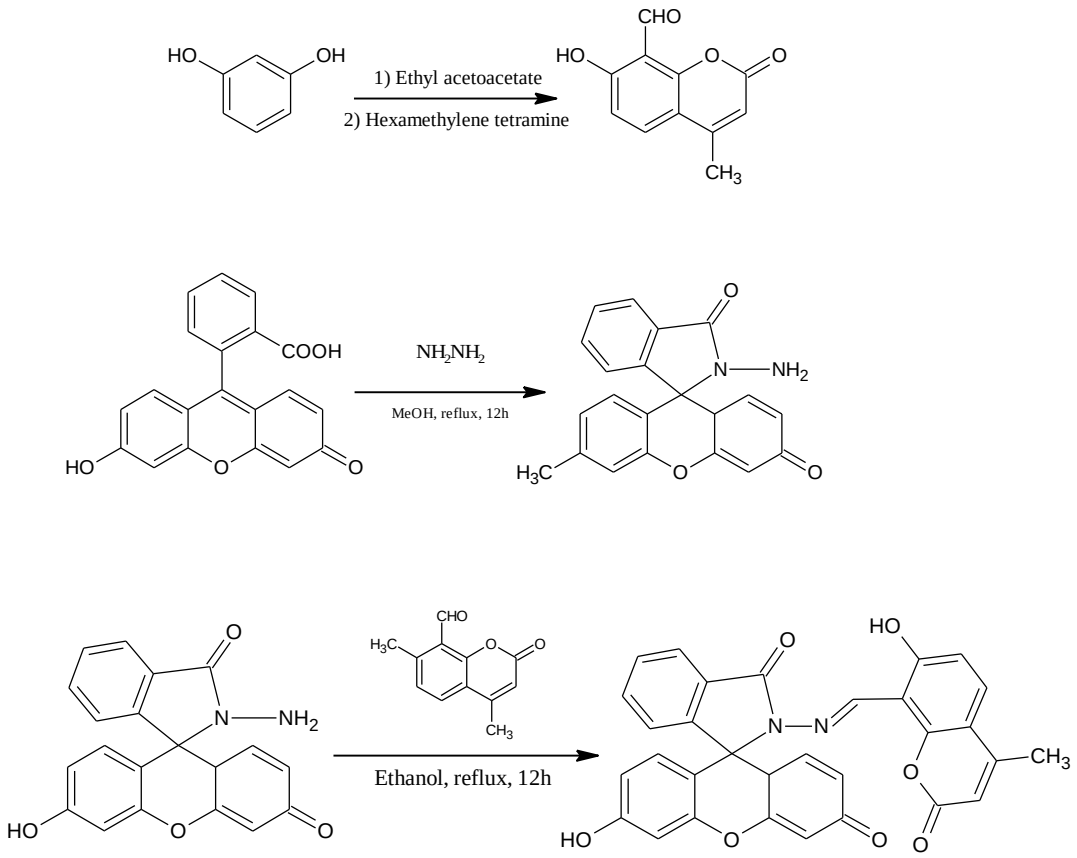
Nagano et al. developedfluorescent Zn^{2+} sensor molecules that possess faster formation of complexes and then even better selectivity. The four nitrogen atoms of the acceptorN,N-bis(2-pyridyl methyl) ethylene-diamine form a co-ordination complex when Zn^{2+} is being added to the molecule that hampers photo-induced electron transfer(PET) process to xanthene from amino group, and this results in strong fluorescence and thus Zn^{2+} is being monitored and imaged and even this was the only molecule developed that could distinguish between Cd^{2+} and Zn^{2+}.[18]

SCHEME 13:



An et al. designed and synthesized a fluorescent sensor, 7-hydroxy-4-methylcoumarin-8-carbaldehyde-(fluorescein) hydrazine. Coumarin and fluorescein derivative is used for selective determination of Zn^{2+} and the sensor givesgreat sensitivity , selectively and color change for Zn^{2+} is just because of spiro lactam ring opening power of Zn^{2+}.The detection limit of the probe towards Zn^{2+} is low as 6.54.

SCHEME 14:



Conclusions

In the present review we have tried to list some of the recent research developments in the field of detection of Hg^{2+}, Cu^{2+} and Zn^{2+} in the renewable energy source i.e. water. We expect that this paper will help researchers to develop more fluorescein based metal detectors.

Acknowledgement

This research was supported by the grant from SERB-DST, India (Project: YSS/2015/001237). We thank SERB-DST (India) for providing Research Assistant Fellowship to Ms. Navjot Sandhu to carry out her research work smoothly.

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