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Review Article

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A Decennary Update on Coumarin Derived Fluorescent Nanosensors and Chemosensors for Selective Sensing of Heavy Metal Ions

Aruna[1], Neelam Sharma[1], Suman Swami[2], Ritu Mathur[3], Rashmy Nair[4] and Rahul Shrivastava[1*]

[1]*Department of Chemistry, Manipal University Jaipur, Rajasthan, India*

[2]*Department of Chemistry, Chandigarh University, Punjab, India*

[3]*Department of Chemistry, Zakir Husain Delhi College, New Delhi, India*

[4]*Department of Chemistry, S.S. Jain Subodh P.G. (Autonomous) College, Jaipur, Rajasthan, India*

***Correspondence to:**
Rahul Shrivastava
Department of Chemistry,
Manipal University
Jaipur, Rajasthan, India.
E-mail: chem.rahul@gmail.com

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Abstract

Fluorescent nanosensors are capable of sensitive and selectively sensing target heavy metal ions under physiological conditions. In recent years, these sensors have attracted enormous interest as they offer outstanding features such as high selectivity, simplicity, extraordinary sensitivity, simple manipulations, rapid response rate, low cost, facile visualization real-time detection, and spatiotemporal resolution. Generally, fluorescent chemosensors exhibit significant noticeable changes in their physicochemical properties upon interaction with target guest analytes and generate detectable fluorescent signal. In the previous times, a wide range of fluorescent nano-chemosensors with sensing capabilities have been designed and evaluated for sensing purposes. Coumarins are a family of 2H-chromen-2-one scaffold, generally found in plants in nature. In recent years, coumarin scaffold has been extensively utilized in designing of fluorescent chemosensors because of its high fluorescence quantum yield, stable and strong fluorescence emission, excellent biocompatibility, low toxicity, and good structural flexibility. This review article emphasis on decennary development of coumarin derived fluorescent and nano-chemosensors for metal ions sensing during the time of 2013 - 2022. This piece of review article could facilitate the scientific community for the advancement of more efficient fluorescent chemosensors and nano-chemosensors for exciting wide range applications in the future.

Keywords

Coumarin, Fluorescent sensors, Nano-chemosensor, Sensing, Heavy metal ions

Introduction

Metal ions play a crucial role in many industrial, environmental, and biochemical purposes. For example, some metal ions like Cu^{2+}, Al^{3+}, Zn^{2+}, Fe^{2+}, etc., are necessary for variety of enzymatic reactions and biological processes in the human body whereas metal ions like Hg^{2+}, Pb^{2+} and Cd^{2+} are toxic and hazardous for human health and environmental [1]. For instance, copper is the third most essential transition element in biological system and plays an important role for human nervous system and physiological process. It was found that although copper toxicity is quite low, its deficiency can cause growth and metabolism problems. Imbalance amount of Cu^{2+} ions cause severe disease like Wilson's disease and Alzheimer's disease [2]. In view of remarkable importance of copper ion, WHO (World Health Organization) restricts 30 μM Cu^{2+} in drinking water and suggests that people' daily intake be limited to 10 - 12 mg [3]. Same way, aluminum, the most common metal in the earth's crust, is

widely utilized in a wide range of applications from cookware to medicine. Increased use of aluminum-containing items could lead to an accumulation of metal in the environment, which could have negative consequences. Aluminum ion caused several diseases such as Parkinson's, amyotrophic lateral sclerosis as well as Alzheimer's disease, among several other diseases [4]. Similarly, unlimited levels of lead generate powerful neurotoxic effects, disrupting brain development, causing behavioral issues, and slowing nerve conduction speeds in human body [5-7]. In addition, cardiovascular, muscle paralysis, neurological, irritability, hypertension, and developmental issues, mental retardation, are also some of major health problems caused by lead ions, especially in children. The nondegradable nature makes pollutant in environment that is difficult to detoxify by biological or chemical methods [8]. The WHO has set the maximum acceptable limits for lead ion is 0.010 mg/L, respectively [9]. Zinc ion is an important transition metal ion in inhuman body and has play important role in cellular metabolism, gene expression, apoptosis, and neurotransmission, among other biological processes [10, 11]. Neurodegenerative illnesses such as cerebral ischemia and Alzheimer's disease have also been linked to Zn^{2+} deficiency [12]. One of the most dangerous heavy metals is mercury, which can be found in divalent compounds and cations in a wide range of waste. Even at low concentrations, Hg^{2+} in both organic and inorganic molecules can easily enter biological membranes and cause damage to the organism [13]. The Hg^{2+} ion is corrosive and carcinogenic, and it has a high level of cellular toxicity [14]. As a result, Hg^{2+} levels must be strictly controlled [15]. It was found that most metal pollutants do not easily decompose with time thus leading to serious concern for several health and environmental problems [15, 16]. In view of deleterious effects of heavy metal ions, it is essential to find out an effective and easy methodology/tool for determine heavy metal ions for protection of environment and human health [17]. It was found that number of effective electroanalytical and spectrophotometric techniques like inductively associated plasma mass spectrometry, mass spectroscopy, emission spectroscopy, atomic absorption techniques are successfully used for detecting heavy metal ions [18]. Although, all these techniques are capable for detecting target species with high sensitivity and selectivity but also associated with some limitations like highly expensive set up, time consuming methodology, difficult to understand, not ideal for in-situ analysis. As a result, rapid, less expensive, and ideal for *in-situ* techniques are required for real time sensing of heavy metal ions for wide and used applications. It was envisaged that detection through nanoparticle and organic molecules-based sensors are one of the best methods since they offer distinguishing features like high sensitivity and selectivity [19, 20], rapid reaction rate, [21] simple manipulations, low-cost techniques [22], real-time detection, [23], easy visualization [24, 25] and spatiotemporal resolution [26].

Generally, chemosensors are designed by linking binding and signaling subunits by suitable spacer. The binding subunits are used to bind target species whereas signaling subunits expresses binding event in terms of spectroscopic/visual changes. The binding characteristic of designed sensor can be fine tune as per requirement by varying structure features of both binding and signaling subunit. In past decade, number of signaling fluorophores subunit have been explored for development of fluorescence-based chemosensors including cyanine [27], fluorescein [28], boron-dipyrromethene [29], 1,8-naphthalimide and rhodamine [30-33] with appropriate recognition subunit. At the same time, nanomaterials have been widely used in the development of sensors with improved features. These nanomaterials not only serve as receptors for specific metal ions but also produce strong signals for detection purposes. It was found that most of the time, nanoparticles serve as a signaling sub-unit for a variety of organic and biochemical ligands. Therefore, sensitivity and selectivity towards target molecule researchers can be improved by employing organic molecules as the sensing components. The detailed literature review revealed that in the past decade, coumarin derivative-based fluorescence sensors and coumarin nano-chemosensor were widely explored for sensing of toxic metal ions [34]. This review article emphasis on decennary development of coumarin derived fluorescent chemosensor and nano-chemosensor for selective detecting of heavy metal ions during the period of 2012 - 2022. The review article arranged under sections of coumarin brief introduction, metal ion sensing properties of coumarin-based chemosensors for heavy metal ions with brief discussion on synthesis of chemosensors and advantages of chemical transformation. The article also supports the advancement of more efficient fluorescent chemosensors for exciting wide range applications in the future. Coumarins (2H-chromen-2-one) generally consists of a benzene with fused pyrone substituted with carbonyl group at second position as shown in figure 1.

Coumarin was isolated from Tonka beans for the first time in 1820, and in 1882 W. H. Perkin chemically synthesized via heating of sodium salt of salicylaldehyde with acetic acid [35, 36]. High fluorescence quantum yield, stable and strong fluorescence emission, excellent biocompatibility, low toxicity and good structural flexibility, chelation properties, and enough replacement sites on the coumarin make it to be potential scaffold for sensor molecules for recognition of heavy metal ions. The parent structure of coumarin (benzopyrone) is generally synthesized by four basic methods: (a) Perkin synthesis; (b) Wittig synthesis; (c) Pechmann synthesis; (d) Knoevenagel synthesis as shown in figure 2 [37].

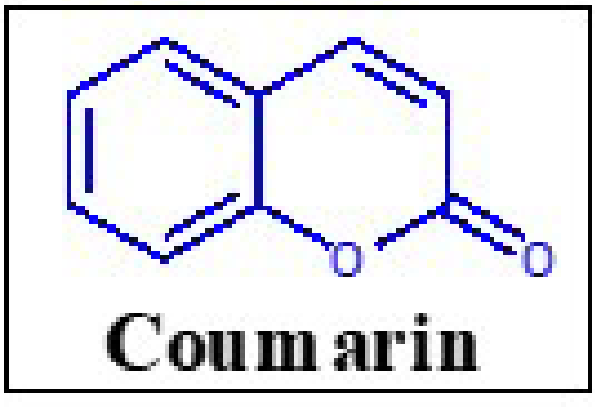

Figure 1: Coumarin chemical structure.

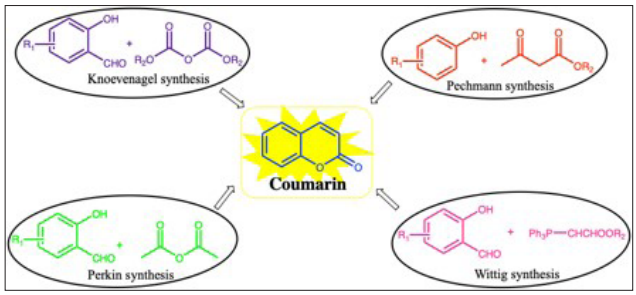

Figure 2: General approaches for the synthesis of coumarin [37].

Coumarin Derived Fluorescent Nano-chemosensor for Sensing of Metal Ions

Owing to impressive properties of nanoparticles such as huge surface area, easier modification, good stability, and extraordinary electronic, and optical properties, nanoparticle-coumarin hybrid nano (probe 1) extensively utilized for heavy metal ion sensing. For instance, ratio metric fluorescent carbon dots were created for selective Cu^{2+} ion detection by grafting, 7-diethylaminocoumarin-3-carbohydrazideon on glyoxylic acid-modified carbon dots, which then underwent an amidation reaction to detect the Cu^{2+} ion non-organic medium. In this glyoxylic acid-modified carbon dots, glyoxylic acids are covalently fused on hydroxyl groups of carbon dots. The 0.21 M limit of detection (LOD) was shown by synthesized carbon dots as depicted in figure 3 [38].

Further, a lanthanide-functionalized magnetic nanoparticles based fluorescent probe 2 was synthesized for ultrasensitive-detecting and effectively separating the Cu^{2+} in the aqueous solution. Such multifunctional nanoparticles exhibit good sensing capabilities for Cu^{2+} ions over different other metal-ions with 0.1 nM detection limit. The distinctive red fluorescence of europium was quenched by contact with Cu^{2+} with remarkable color changes (Figure 4) [39].

A new eco-friendly probe 3 based halloysite nanotube (HNTs) appended with coumarin was synthesized by Su and his coworkers for detection of Zn^{2+} ions. In the reported sensor. The carbaldehyde functionalized hydroxy coumarin is attached to the surface of aminated-HNTs through condensation reaction. In these synthesized nanotubes, hydroxy coumarin acts as a fluorescence donor whereas HNTs act as acceptor as depicted in figure 5. Interestingly, it was observed that encounter of Zn^{2+} ion, CHNTs, trigger fast fluorescence "turn on" response because of hydrogen bonding interaction between zinc, phenolic oxygen and imine nitrogen which quench fluorescence response. Due to its excellent selectivity, efficiency, and hydrolytic durability the novel chemo-sensor may identify Zn^{2+} ions from other possibly conflicting metal ions [40].

In continuation, coumarin-doped Pdot probe 4 was constructed for the ratio metric fluoride ion sensing in H_2O medium. In the synthesis of sensor, initially hydroxyl group of coumarin (CA) was protected by tert-butyldiphenylsilyl (TBDPS)/triisopropylsilyl (TIPS) to produce TBDPSCA/TIPSCA which was blended with poly(2,5-di(30,70-dimethyloctyl)phenylene-1,4-ethynylene) in tetrahydrofuran

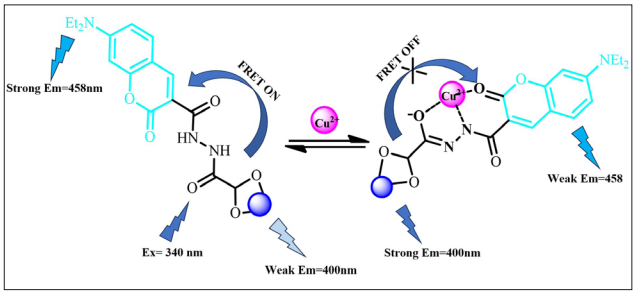

Figure 3: The sensing of coumarin based carbon dots probe 1 for Cu^{2+} detection.

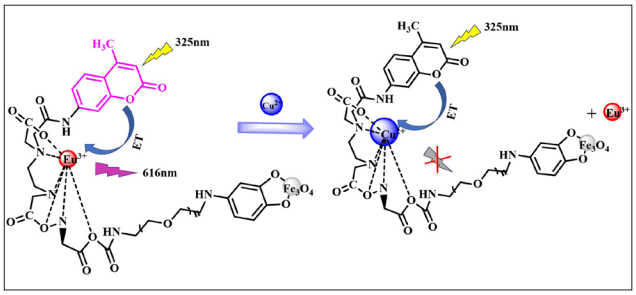

Figure 4: The Cu^{2+} metal ions sensing via magnetic nanoparticles based fluorescent probe 2.

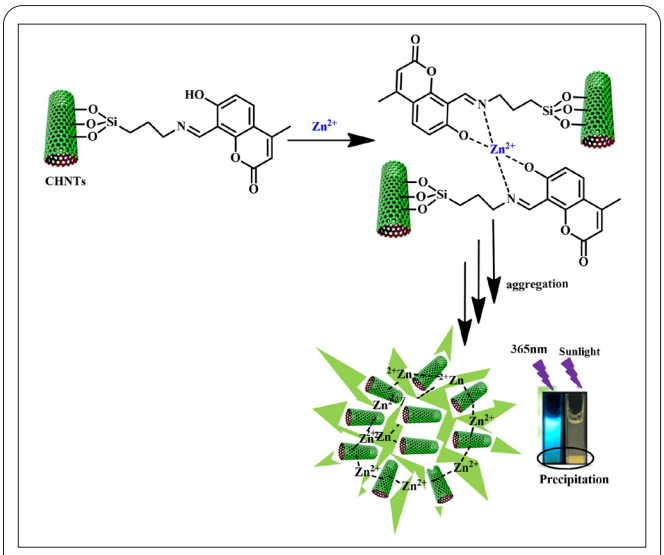

Figure 5: Aggregation mechanism of CHNTs probe 3 against Zn^{2+} ion.

for synthesis of coumarin-doped Pdots as depicted in figure 6. Further, to prevent possible leakage of trapped coumarin dyes, a layer of polydiacetylenes was added to the Pdots. The coumarin-doped Pdot was than investigated for fluoride ion sensing. It was found that during interaction with fluoride ions, small amount of fluoride ions enters in matrix of Pdot and remove silyl group's protection of TBDPSCA which result coumarin enhancement of fluorescence response (Figure 6) [41].

Another, interesting and less expensive hybrid coumarin-graphene based fluorescent probe 5 was synthesized for optical sensing of copper ions. Authors reported that interaction between graphene and coumarin moieties reduced the fluorescence response and constructed turn-on sensor unit.

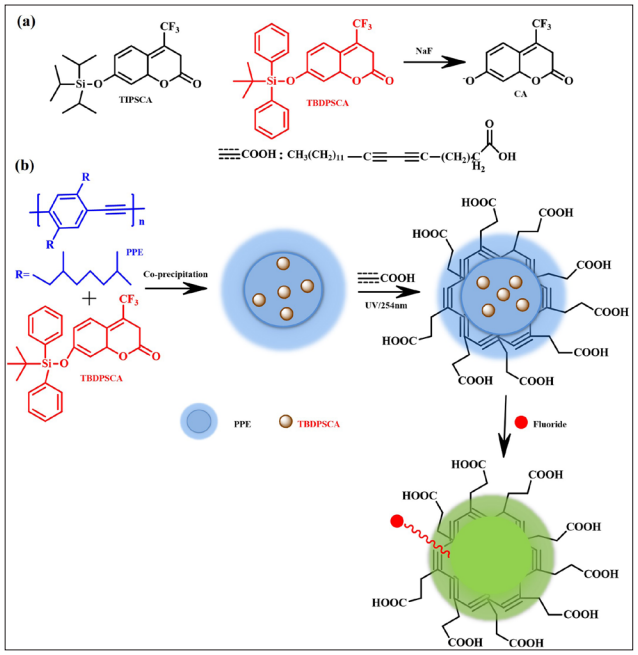

Figure 6: Schematic representation of the detecting of F^- (fluoride) by probe 4, coumarin dye-doped PPE Pdots.

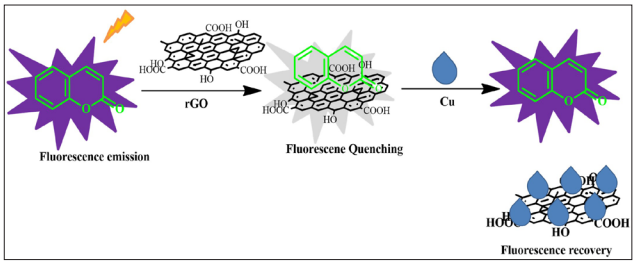

Figure 7: Sensing mechanism for the fluorescent probe 5 to detect Cu^{2+} ions.

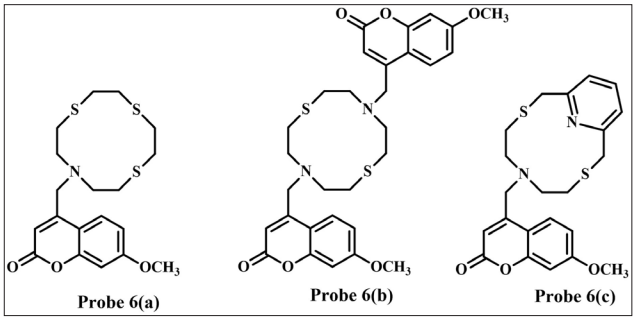

Figure 8: Different types of fluorescent probe 6.

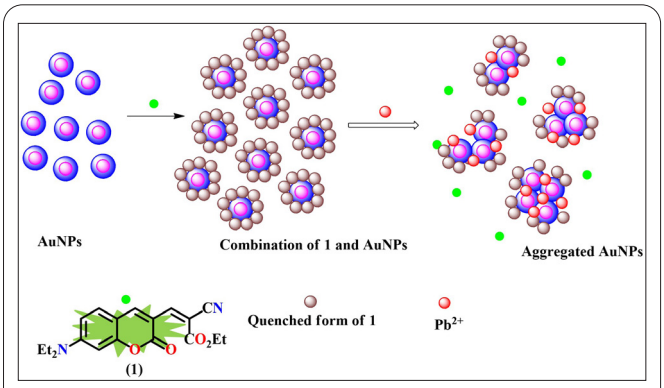

Figure 9: Proposed sensing mechanism of fluorescence quenched AuNPs/1 probe 7 for detection of Pb^{2+} ions.

It was observed that encounter of copper ion with reported sensor molecule, reduced intensity was recovered because copper ion has higher affinity to graphene as compared to coumarin molecule as shown in figure 7 [42].

Further another type of fluorescent molecular probe 6 based on coumarins was synthesized for the sensing of mercury ion using thia-aza macrocycles as a receptor unit as depicted in figure 8. Probe 6 was used for detecting Hg^{2+} ion *in vitro* by using silica cored nanoparticles as vehicles. The sensors exhibited extraordinary capability for detecting Hg^{2+} ions in water and can image Hg^{2+} ions in Cos-7 cells when they are embedded in silica core-polyethylene glycol shell nanoparticle or supported on membranes composed of polymers made of polyvinyl chloride [43].

Additionally, Khan and coworkers developed fluorescent gold nanoparticle (AuNPs) and coumarin-based nano probe **7** 3-Amino-2-cynano-3-(7-diethylamino-2-oxo-2H-chromen-3-yl)-acrylic acid ethyl ester@ AuNPs. It was found that reported nanoparticles exhibit lower quantum yield and shorter excitement in polar solvents compared to nonpolar solvents. The AuNPs conjugate nanosensor was employed for Pb^{2+} ion detection through change in color and UV-Vis spectrum. Detailed studies revealed that presence of Pb^{2+} ions result agglomeration of AuNPs which was supported by transmission electron microscope analysis as shown in figure 9 [44].

Another coumarin functionalized Fe_3O_4@SiO_2 nanoparticles was described, as combination is providing large surface area and abundant -OH groups for immobilization process. Alkoxysilanes are difficult to store and coat, and they are vulnerable to hydrolysis. The silica surface is functionalized to address this issue and an organo silane-based on coumarin acts as an organic support structure. Synthesis of terminal alkyne-derived coumarin-based triazole-linked organo silanes utilizing the click technique. The magnetizing silica surfaces illustrated in figure 10 were the anchor for the coumarin-tethered organosilanyl molecule. The synthesized compounds exhibit a high level of specificity for the Hg^{2+} ion [45].

For the detection of Ag^+, Hg^{2+}, and silver nanoparticles, a novel luminous coumarin derivative probe 8 was synthesized. It was found that compared to other Ag^+ and Hg^{2+} chemosensors, coumarin dithioate derivatives have some advantages, including quick response, superior choice, and lower LOD. After selective complexation with Ag^+, Hg^{2+}, and silver nanoparticles, fluorescence was increased by factors of 5 to 12 times. The fluorescent probe 9 serves as an excellent and rapid selective "off-on" fluorescent sensor. Two sulfur atoms are found in each coumarin molecule in the probe in study. This affects how quickly the probe binds to Hg^{2+} and influences the ratio of the chelation product formed. The probe's sulfur atoms affect the binding properties and stoichiometry of the chelation product with Hg^{2+}, but the method utilizing this probe has the benefits

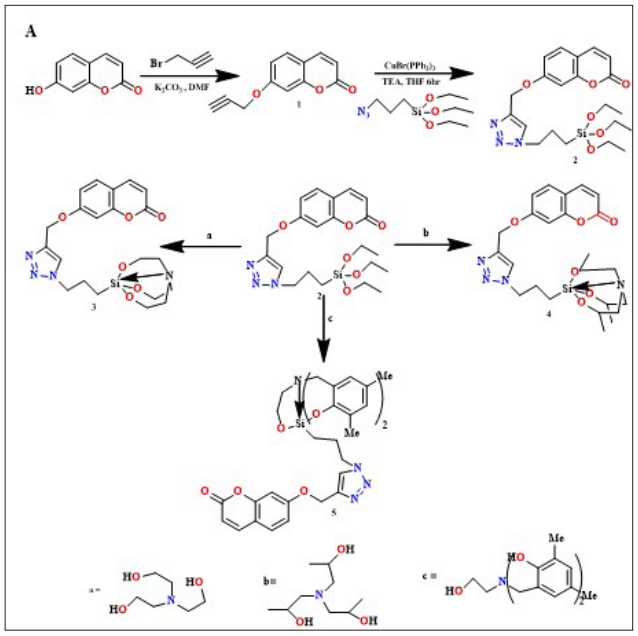

Figure 10: (**a**) synthesis of coumarin derived organosilatranes and (**b**) synthesis of probe 8.

of a wide measurement range, low detection limits, simplicity, and time-saving capabilities (Table 1). The fluorescent probe being discussed is designed to detect certain substances rapidly and selectively by changing their fluorescence signal (Figure 11) [46].

Coumarin Derived Fluorescent Chemosensor for Sensing of Metal Ions

Coumarin scaffold has been widely used to create fluorescent chemosensors for heavy metal ions due to high fluorescence quantum yield, robust and stable release of fluorescence, great bio compatibility, low toxicology, and remarkable structural adaptability of coumarin. To detect Cu^{2+} ions in phosphate buffered saline (PBS) as well as acetonitrile solution buffers, a novel fluorescent CHT probe 10 was created by exploiting a Schiff base fusion process. To generate favorable photophysical properties of the coumarin derivative, 2-benzothiazolinonehydrazone was connected to coumarin

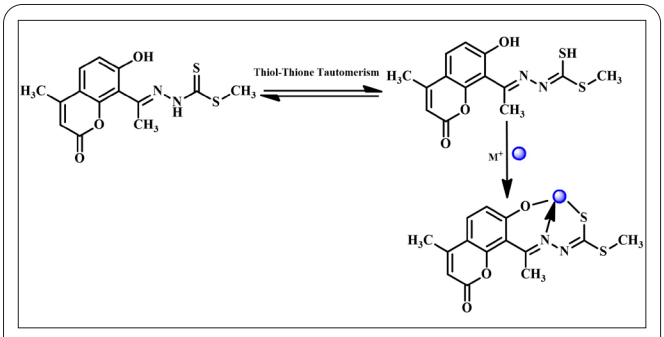

Figure 11: The binding model of synthesized compound probe 9 with metal ion.

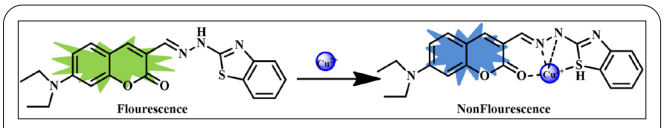

Figure 12: Chelation with the Cu^{2+} ions quench the fluorescence CHT probe 10.

derivative 7-(N,N-diethylamino) coumarin-3-aldehyde to provide sensor molecules. It was observed that when Cu^{2+} ions were interacting with reported sensor, a significant fluorescence quenching at 540 nm was recorded (Figure 12) [47].

Additionally, a fluorescent-colorimetric chemosensor probe 11 derived from coumarin and methionine methyl ester was created to measure the Cu^{2+} ion. It was discovered that the Cu^{2+} ion interaction changed color of sensor solution along with improved brightness in fluorescence response. The detection limit for Cu^{2+} computed by the authors was 1.84 x 10^{-7} M, which was significantly less than the recommendations of the United States Environmental Protection Agency (US EPA) (20 M) and WHO (31.5 M) as shown in figure 13 [48].

Furthermore, Arslan et al. [49] designed a probe 12 for Cu^{2+} ions detection through interesting "turn-on-off" fluorescence signal mode. The synthesized probe 12 HMAC (6,7-dihydroxy-3-(4-(trifluoro)methylphenyl)coumarin) is straight forward technique for copper on detection that exhibits realistic potential for monitoring of Cu^{2+} ion. The LOD was found to be 24.5 nM, which is comparable to the recommendation of WHO. The Job's approach and ESI-MS technique was used to determination of the stoichiometry

Table 1: An overview of coumarin derived fluorescent nano-chemosensor for sensing of metal ions.

Entry	Fluorescent probe	Metal	Working system	$\lambda_{ex}/\lambda_{em}$ (nm)	LOD	Ref.
1	Probe-1	Cu^{2+}	HEPES buffer (pH = 7.4)	340/458	0.21 M	[38]
2	Probe-2	Cu^{2+}	Aqueous solution	325/616	0.1 nM	[39]
3	Probe-3	Zn^{2+}	CH_3CN/H_2O (1:9, v/v)	365	16 mg/g	[40]
4	Probe-4	F^-	Water	440/520	-	[13]
5	Probe-5	Cu^{2+}	MeCN and water	392/404	2 x 10^{-15} M	[24]
6	Probe-6	Hg^{2+}	$MeCN/H_2O$ (4:1 v/v),	319/405	9.1 x 10^{-9} M	[43]
7	Probe-7	Pb^{2+}	Aqueous solution	424/520	1.2 x 10^{-8} M	[44]
8	Probe-8	Hg^{2+}	CH_3CN-H_2O (9/1, v/v)	Em370	0.7463 x 10^{-3} M	[45]
9	Probe-9	Ag^+, Hg^{2+}, AgNPs	Methanol/water (1:1, v/v)	339/520 339/509 339/510	0.029 x 10^{-5} mol/L, 0.04 x 10^{-5} mol/L, 0.04 x 10^{-12} mol/L	[46]

of the HMAC-Cu^{2+} adduct which was found to be 1:1 stoichiometry. The reported binding mode of HMAC with copper ion is shown in figure 14 [49].

Another type of coumarin based fluorescent chemosensor (BENZPYR) probe 13 was reported by Mani et al. [50] which was successfully fabricated via condensation of 2-hydrazinobenzothiazole with N,N-diethylamino-3-acetyl coumarin and was found to be selective for determination of Cu^{2+} in DMF medium as compared to other tested metal ions. The BENZPYR shows "turn off" response with copper ion through intramolecular charge transfer and chelation phenomenon. In addition, the color of BENZPYR altered from yellow to wine red after interaction of Cu^{2+} ions owing to metal to ligand energy transfer and metal ion d-d transition as depicted in figure 15 [50].

A novel (Z)-2-((7-(diethylamino)-2-oxo2H-chromen-3-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) ethane sulfonic acid probe 14 was constructed for the determination of Hg^{2+}. The reported probe 14 was designed to incorporate diethyl-aminocoumarin fragment with a unit of rhodanine via desulfurization reaction. Whereas the thiocarbonyl group would be specifically responsible for recognizing the Hg^{2+} ions (Figure 16) [51].

Huang et al. [52] developed a novel coumarin derived colorimetric fluorescent probe 15 for sensing of Hg^{2+} with LOD is 2.78 x 10^{-8} M. They reported that synthesized probes only responded with mercury ions in presence of other metal ions in terms of color and fluorescence changes as shown in figure 17 [52].

In another report, Mahata et al. [53] synthesized a hybrid coumarin and pyrene probe 16 by reaction of coumarin amine with pyrene aldehyde. The detection ability of reported sensor was examined for various heavy metal ions. The results revealed that sensor showed extreme selectivity for determination of trivalent ions like Cr^{3+}, Al^{3+}, and Fe^{3+} at physiological pH which make it appropriate for practical applications. The interaction of sensor with Al^{3+}, Fe^{3+} and Cr^{3+} were found to be 1:1 with high binding constant. The reported sensor exhibits an interesting "turn-on" response during encounter of Cr^{3+}, Al^{3+}, and Fe^{3+} due to inhabitation of PET process as shown in figure 18. The detection limits were found for 1.15 µM, 0.79 nM, and 1.28 µM for Cr^{3+}, Al^{3+}, and Fe^{3+} ions, respectively (Figure 18) [53].

Athiadiazole and coumarin based dual chemosensor probe 17 was designed and synthesized by Xu and his group. The synthesized sensor showed simultaneous dual function chemosensing for both Hg^{2+} and Cu^{2+} via change in colorimetric responses and fluorescence changes in comparison with other metal ions. The synthesized CTT exhibits turn-on fluorescence response with remarkable fluorescence enhancement with limits of detection of 2.96 x 10^{-7} M (Figure 19) [54].

In another report, a coumarin–triazole-based sensor 4-((1-(2-oxo-2H-chromen-4-yl)-1H-1,2,3-triazol-5-yl) methoxy)-2H-chromen-2-one was developed to identify Pb^{2+} ion in aqueous medium as low concentrations of Pb^{2+} is very harmful for human health causes neurological, cardiovascular,

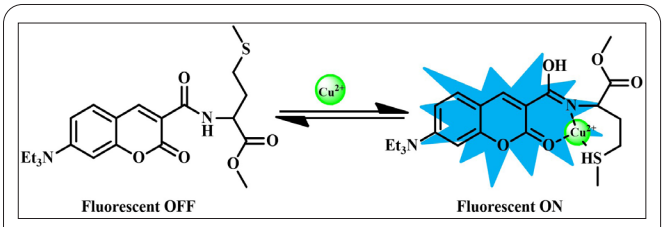

Figure 13: Sensing mechanism for Cu^{2+} with coumarin based chemosensor probe 11.

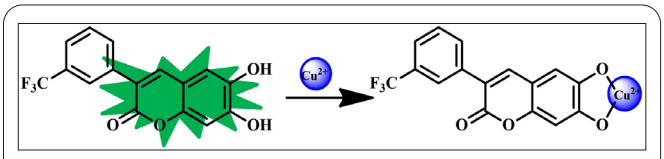

Figure 14: binding mechanism of HMAC probe 12 and copper complex.

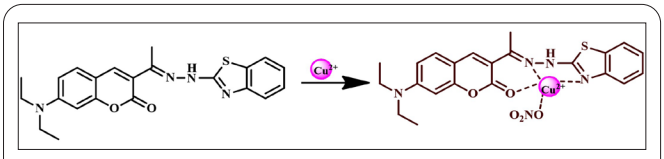

Figure 15: Sensing mechanism of Cu^{+2} ion using coumarin based fluorescent chemosensor (BENZPYR) probe 13.

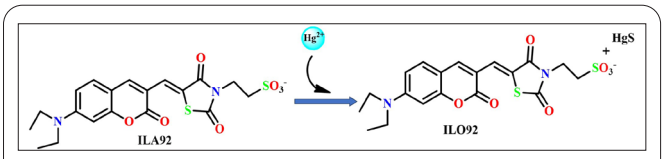

Figure 16: Desulfurization reaction proposed in between mercury ion and ILA92 probe 14.

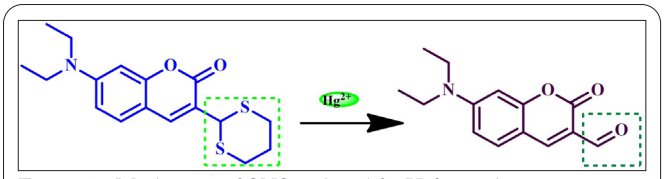

Figure 17: Mechanism of CNS probe 15 for Hg^{2+} metal ion.

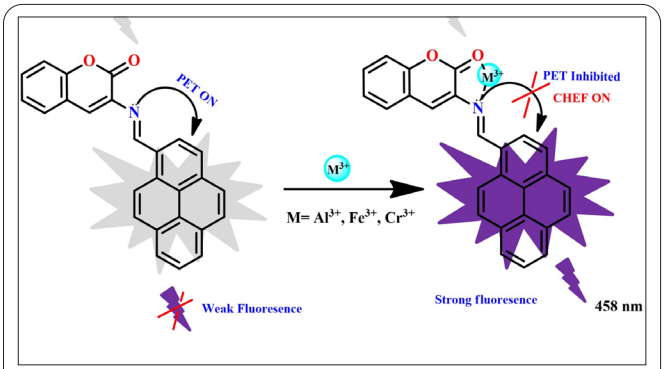

Figure 18: The sensing probe 16 for Al^{3+}, Fe^{3+}, and Cr^{3+}.

developmental, and reproductive disorders. It was reported that the intensity of fluorescence reported sensor was significantly quenched by addition of Pb^{2+} and clear color change was observed. Detailed fluorescence studies revealed that sensor binds with Pb^{2+} ion in 1:1 binding stoichiometry with 1.9

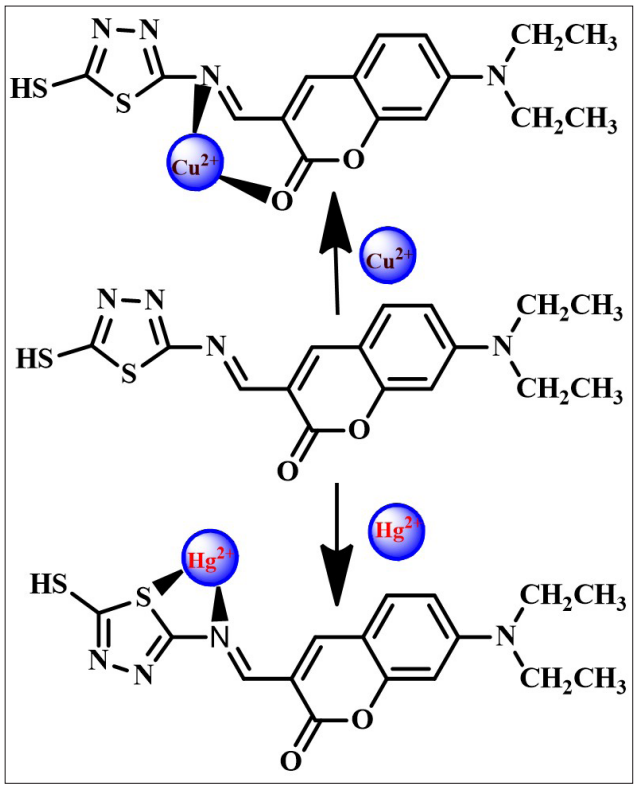

Figure 19: The mechanism shows the binding interactions between CTT probe 17, Cu^{2+}, and Hg^{2+}.

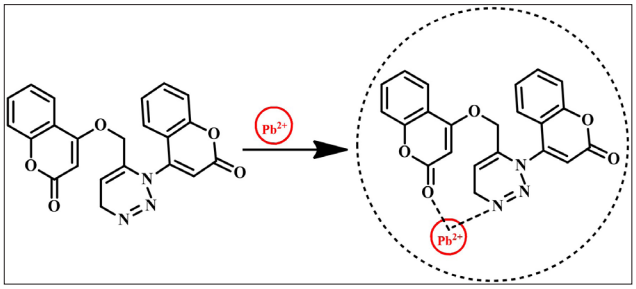

Figure 20: The mechanism of compound for Pb^{2+} through probe 18 [8].

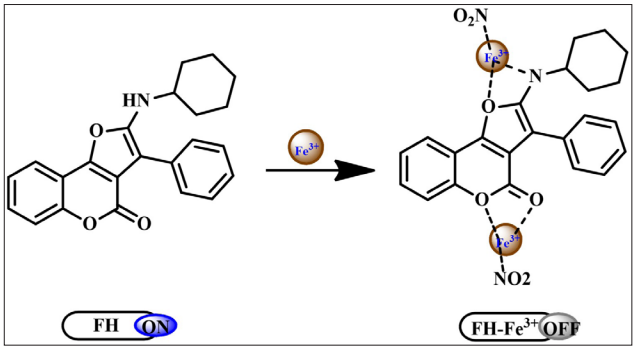

Figure 21: The sensing of Fe^{3+} through FH probe 19.

nM detection limit. Additionally, test strips impregnated with reported sensor were also produced for effective detection of Pb^{2+} for practical application (Figure 20).

Sarih et al. [55] synthesized furo[3,2-c]coumarin-derived fluorescence probe 19 via 4+1 cycloaddition between 4-hydroxycoumarinand substituted benzaldehyde for selective detection of Fe^{3+} ion. The reported sensor shows selective and instant turn-of fluorescence response to Fe^{3+} over other thirteen tested metal ions in 10% MeOH-H_2O solution that was attributed towards a transfer of charge mechanism. The binding stoichiometry and the binding constant of sensor with Fe^{3+} was found to be 1:2 and 5.25 x 10^3 M^{-1}, respectively (Figure 21). Additionally, novel sensor exhibits LOD of 1.93 µM which was insufficient compared to the US EPA recommendations (5.37 µM). The potential of sensor was also successfully carried out for detection of Fe^{3+} in samples of tap water illustrating the practical use [55] (Table 2).

Like this, quinoline carboxamide-coumarin was used to build and create a specific "turn-off" fluorescence probe 20 for Al^{3+} detection. The described sensor possesses diethylamino

Table 2: An overview of coumarin derived fluorescent chemosensor for sensing of metal ions.

Entry	Fluorescent probe	Metal	Working system	λ_{ex} / λ_{em} (nm)	LOD	Ref.
1	Probe-10	Cu^{2+}	PBS and acetonitrile buffer solutions	458/540	-	[47]
2	Probe-11	Cu^{2+}	HEPES buffer/CH_3CN (40:60, v/v)	418/460	1.84 x 10^{-7} M	[48]
3	Probe-12	Cu^{2+}	CH_3CN/HEPES (95/5, v/v)	364/458	24.5 nM	[49]
4	Probe-13	Cu^{2+}	HEPES buffer, 1% DMSO	420/572	40 nM	[50]
5	Probe-14	Hg^{2+}	HEPES-DMSO (99/1 v/v; pH 7.0)	530/645	15.6 x 10^{-6} M	[51]
6	Probe-15	Hg^{2+}	(1:1, THF/H_2O V/V)	490/550	2.78 x 10^{-8} M	[52]
7	Probe-16	Al^{+3}, Fe^{3+}, Cr^{3+}	MeOH: aqueous HEPES buffer (6:4, v/v).	353/458	0.79 nM, 1.28 µM, 1.15 µM,	[53]
8	Probe-17	Cu^{2+}, Hg^{2+}	-	-	2.96 x 10^{-7} M	[54]
9	probe-18	Pb^{2+}	PBS (20 mM, pH 8.01:9 DMSO/H_2O (v/v))	390/462	1.9 nM	[54]
10	Probe-19	Fe^{3+}	10% MeOH-H_2O solution	375/492	1.93 µM	[55]
11	Probe-20	Al^{3+}	MeCN/H_2O (95:5)	432/475	-	[56]
12	Probe-21	Ni^{2+}	THF	462.5	2.1 x 10^{-11} M	[57]
13	Probe-22	Pb^{2+}, Hg^{2+}	HEPES buffer solution	420 nm	10.5 and 8.3 nM	[58]
14	Probe-23	Zn^{2+}	Aqueous solutions	475/510	6.1 x 10^{-8} M	[59]
15	Probe-24	Ga^{3+}	Tris-HCl aqueous buffer solution	344	4.88 x 10^{-2} µM	[60]
16	Probe-25	Pd^{0}	PBS solution	412/450	4.88 x 10^{-2} µM	[61]
17	Probe-26	Hg^{2+}	DMSO	354/450	0.020 µmol/L	[62]

group at 7- position at coumarin moiety which causes it to glow blue and have a high fluorescence quantity. Al^{3+} ion response from the sensor was highly sensitive and discriminates. Furthermore, density functional theory simulations and chemometric techniques supported the presented potential quenching process (Figure 22) [56].

An acylhydrazone coumarin based fluorescent chemosensor probe 21 was synthesized by Lu et al., for the determination of Ni^{2+} ions. The detailed experimental results demonstrated high selectivity and low LOD 2.1 x 10^{-11} M towards Ni^{2+} ions. The Job's plot and mass spectrum proved the 2:1 binding with sensor with Ni^{2+} ion. The sensor was used for detection of Ni^{2+} in water and in real environmental samples (Figure 23) [57].

A 4-(diethylamino) salicyl aldehyde incorporated coumarin based chemosensor probe 22 was designed and fabricated for Pb^{2+} and Hg^{2+} in aqueous medium through photo-induced electron transfer processes. The emission signal of synthesized sensor was remarkably quenched after interaction with Hg^{2+} and Pb^{2+} ion. The binding behaviors of sensor towards Pb^{2+}/$Hg^{2+}$are studied in detail using spectroscopic studies and density functional theory calculations. The synthesized sensor showed excellent sensitivity, water solubility and high selectivity with 10.5 and 8.3 nM LOD for Pb^{2+} and Hg^{2+} in aqueous medium, respectively (Figure 24) [58].

Hu et al. [59] constructed a simple coumarin based chemosensor probe 23 which showed rapid turn-on fluorescence response only for Zn^{2+} ion in aqueous solutions. It is noticeable that the reported sensor acts as a molecular switch that was continually controlled through Zn^{2+} and EDTA. Detail spectroscopic studies revealed that sensor binds Zn^{2+} ion with binding constant 2.9 x 10^3 M^{-1} and about 6.1 x 10^{-8} M detection limit. The chelation of sensor with Zn^{2+} lead an effective suppression of the C=N group's PET process which results strong fluorescence (Figure 25) [59].

Similarly, Wang et al. [60] designed coumarin Schiff-base derived novel probe 24. The synthesized sensor showed remarkable selectivity as well as sensitivity towards detection of Ga^{3+} ion over other rested ions in aqueous medium. It was observed that sensor bind with Ga^{3+} in 1:1 binding stoichiometry. They also found that response time for Ga^{3+} detection is only two minutes (Figure 26) [60].

Liu et al. [61] reported off-on coumarin-based probe 25 for rapid sensing of palladium ion in PBS solution. It was observed that after addition of palladium in solution of sensor, both fluorescence bands at 450 nm and absorption band at 412 nm rise sharply. The addition of allyl carbonate ester destroys the intramolecular charge transfer process, and the sensor becomes nonfluorescent. The impact of Pd^0 on the probe can cause the conjunct allyl carbonate ester to separate (Figure 27) [61].

Hande et al. [62] prepared mercury ion imprinted polymer through radical polymerization of N-[4-(2-Oxo-2H-chromen-3-yl)-thiazol-2-yl]-acrylamide and ethylene glycol dimethacrylate (cross-linker) for selective detection of mercury ion. The reported polymer was characterized by ^{13}C NMR spectroscopy, FE-SEM, FTIR, BET and XPS. These studies confirm the involvement of functional groups in complexation with mercury ions. The fluorescence studies exhibited 0.020 µmol/L detection limit with 0.05 - 1.2 µmol/L

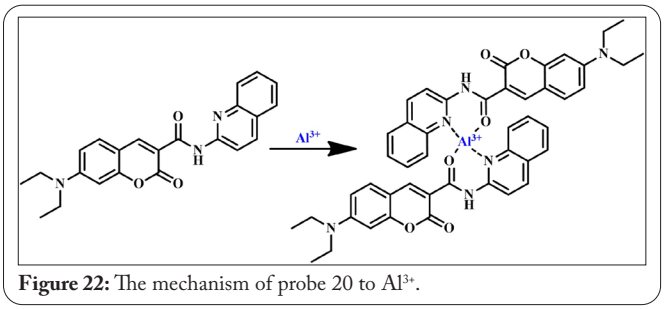

Figure 22: The mechanism of probe 20 to Al^{3+}.

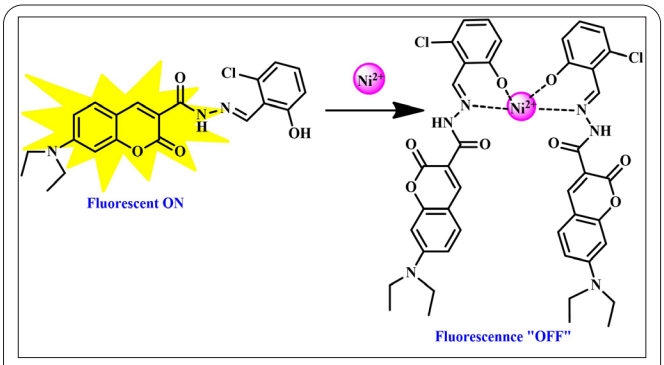

Figure 23: The detection mechanism for Ni^{2+} through probe 21.

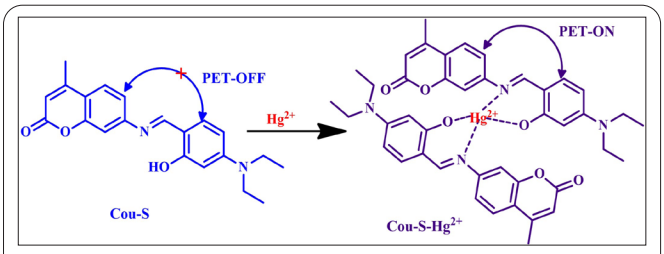

Figure 24: The binding mechanism of Cou-S probe 22 for Hg^{2+} metal ions.

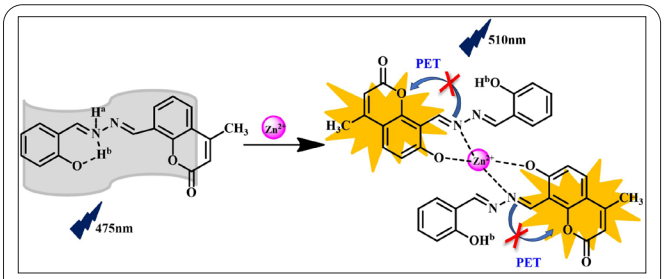

Figure 25: The detection of Zn^{2+} through coumarin group-based azine derivative probe 23.

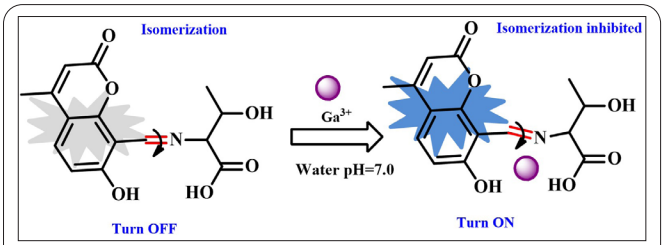

Figure 26: Detection of Ga^{3+} through fluorescent sensor based on coumarin probe 24.

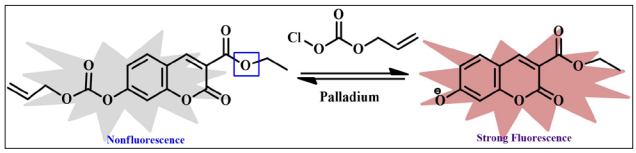

Figure 27: Detection of Pd^0 through fluorescence probe 25 based on coumarin.

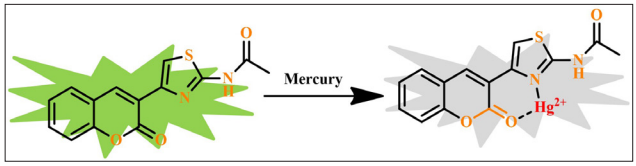

Figure 28: The binding of Hg(II) by coumarin fluorescent probe 26 OC-TAA.

linear range of (Figure 28) [62].

Conclusion

thoroughly review, it has been witnessed coumarins have been widely used as chemosensor including biological sciences, clinical care, environmental monitoring, and detection of metal ions contamination. Coumarin derivatives show a considerable fluorescence enhancement or quenching on complex with heavy metal ions in simple and efficient manner. This type of on–off–on fluorescence detection method was a reversible procedure that could be performed repeatedly with little loss of fluorescence intensity. We anticipate this piece of review could help scientific community to explore the further potential of coumarin-based fluorescence probes and nanosensors, with design selectivity, to create simpler and more efficient applications in many different areas and to improve sensing.

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Conflict of Interest

None.

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