Indole-based Fluorometric and Colorimetric Chemosensors for the Selective Detection of Cu^{2+}: A Brief Review From the Year 2011-2021

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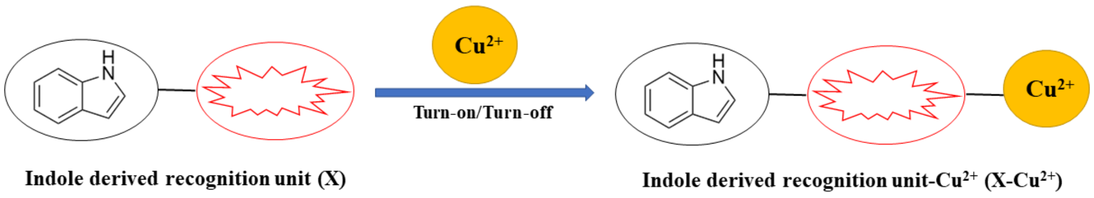
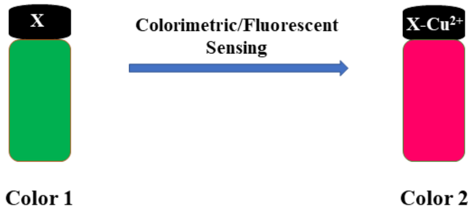
Graphycal Abstract





Abstract

The development of chemosensors has been driven by concurrently advanced research in fluorescence and colorimetric chemosensing. Over the last few decades, the development of copper ion-selective fluorogenic and chromogenic chemosensors has been extensively studied due to their high sensitivity, low cost, and simplicity. They can interact with the metal ion in a unique manner and create measurable color, fluorescence, or redox potential changes. Copper (Cu^{2+}) ion is deemed the third most prevalent transition metal in human beings owing to its various biological and physiological processes. It has drawn a great deal of attention from many researchers in various disciplines such as biology, medicine, and environmental studies. However, an excessive buildup of copper in the body has been linked to several diseases. Thus, more recent research is being focused on developing fluorometric and colorimetric chemosensors for the selective detection of copper ions. Recently, there have been a lot of studies reported in this field of study that describe highly sensitive and sophisticated indole-based chemosensors for various metal ions of interest. In addition, indole derivatives possess inherent fluorescence properties due to their electron-rich nature caused by the π-excessive system of indole, and therefore they can be employed in chemosensors for metal ion detection. Both cations and anions employ it as a molecular recognition system. This review summarizes selective and sensitive Cu^{2+} ion detection accomplished by various indole-based chemosensors between the years 2011 to 2021. Furthermore, sensor design, sensing methods, ligand-metal binding stoichiometry, association constant, and the detection limit by the chemosensors are all summarized and explored.

Keywords: Indole, Fluorescent chemosensors, Colorimetric chemosensors, Cu^{2+}, Turn-on, Turn-off

1. Introduction

Researchers are increasingly interested in designing and synthesis fluorescent and colorimetric chemosensors that are capable of selective detection of specific analytes due to their various applications in biological, chemical, medical, and environmental fields (Yin et al., 2010, Gou et al., 2011). The selectivity and sensitivity of chemosensors in both aqueous and non-aqueous environments are the most important attributes for the detection of metal ions (Xu et al., 2010, Aron et al., 2015, Velmurugan et al., 2015). Chemosensors can be categorized as colorimetric, optical, electrochemical, and piezoelectric sensors based on the type of signaling unit. The most commonly utilized fluorophores and chromophores in the creation of a chemosensor are indole, anthracene, rhodamine, thiourea, anthraquinone, quinone, etc. As a signaling unit, they are connected to an analyte recognition unit and used to detect a variety of ionic and neutral analytes. When the target analyte is recognized, the signaling unit of optical and colorimetric chemosensors exhibits changes in visible color and UV-Vis spectra. These shifts can be used to identify the analyte both quantitatively and qualitatively. Heterocyclic compounds have been frequently used as signaling units in fluorescence-based chemosensors (Mashraqui et al., 2012, Quan et al., 2014).

Copper is the third most prevalent transition metal in humans and has received a lot of attention in recent literature (Krämer, 1998, Mani et al., 2019, Sun et al., 2018, Yang et al., 2013, Aron et al., 2015, Carter et al., 2014). Among various cations, copper (Cu^{2+}) ions are crucial to many biological functions and environmental processes. On the other hand, Cu^{2+} is one of the leading heavy metals involved in environmental pollution. It is a necessary micronutrient in living beings including plants and animals as it engages in a variety of physiological functions and biological processes like respiration, antioxidant defense, and iron metabolism owing to its oxidative and catalytic properties (Muthuraj et al., 2014, Gaggelli et al., 2006, Gangatharan et al., 2018, Sivaraman et al., 2018). However, excess of Cu^{2+} ions causes diseases like Menkes (copper deficiency), Wilson's (copper overload) (Fu et al., 2017, Tang and Cai, 2012), Alzheimer's, and Parkinson's (Guo et al., 2019) neurodegenerative diseases such as familial amyotrophic lateral sclerosis (Meng et al., 2015, Ranee et al., 2018). The extensive usage of copper in the current society has made it a significant metal pollutant. The US Environmental Protection Agency (EPA) mandates that the acceptable amount of copper in drinking water should be lower than 1.3 ppm

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(Bhardwaj et al., 2018a, Bhardwaj et al., 2018b, Wang et al., 2020). Therefore, scientists are focusing their efforts on developing fluorescent and colorimetric chemosensors to detect transition metal ions like Cu^{2+} in biological, pharmacological, and environmental systems (Pal et al., 2014).

The receptor must have a great affinity for the relevant target to be an appropriate fluorometric and/or colorimetric chemosensor to show binding selectivity. Furthermore, there should be no disturbance from the environment in the fluorescence signal to have the signal-selectivity (Xu et al., 2010). For a fluorometric and/or colorimetric chemosensor to be effective in action, it should be able to change the existing fluorescent properties by fluorescence quenching or fluorescence enhancement via the interaction with metal ions in the solution (Rani, 2015, Anger et al., 2006). The metal is recognized by the binding unit which causes the signaling unit to respond with its matching fluorescence spectrum (Zhou et al., 2014). Modification of the signaling subunit and/or the binding subunit allows for the synthesis and designing of chemosensors capable of recognizing various analytes with desirable features (Figure 1). In this review, we particularly focus on the indole-derived fluorogenic and chromogenic chemosensors reported for the detection of Cu^{2+} ions from the year 2011 to 2021.

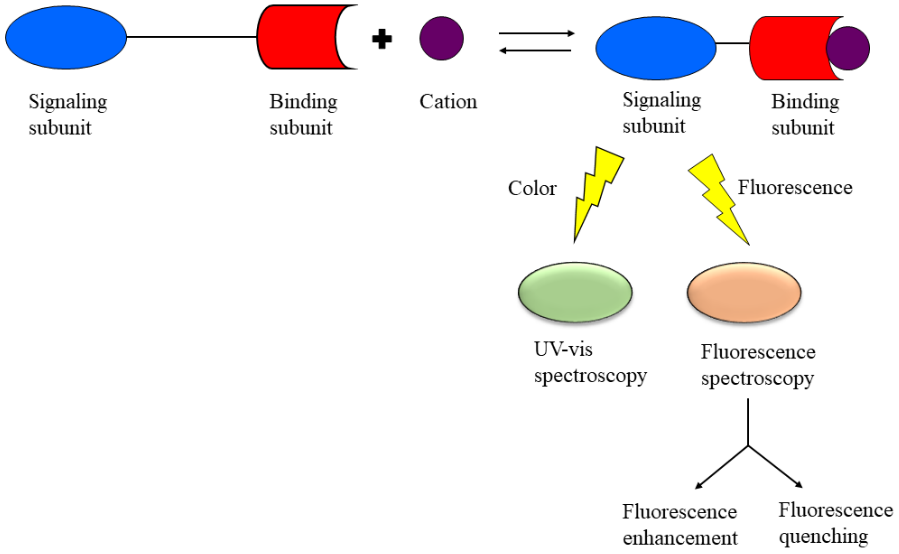

Figure 1. Simplified representation of designing a chemosensor (adapted from ref. (Jali et al., 2021).

2. Indole

Indole is a planar aromatic heterocyclic compound that consists of a benzene ring fused to pyrrole (Sravanthi and Manju, 2016). The indole motifs are present in various biomolecules and natural products such as proteins, alkaloids, and amino acids. Indole systems have sparked a lot of attention in recent literature due to their beneficial applications in biological, chemical, and environmental processes (Sravanthi and Manju, 2016, Kaushik et al., 2013, Zhang et al., 2015, Rahman et al., 2018, Shiri, 2012). Indole-containing molecules are excellent candidates for chemosensors to detect metal ions due to their ability to change the local perturbation and surroundings and to alter the spectral signals such as fluorescence and UV-Vis for a specific analyte

(Bose and Ghosh, 2010). Indole-based chemosensors show inherent fluorescence properties due to their electron-rich π- system. In addition, they are molecular recognition systems for various cations and anions such as Cu^{2+}, Cd^{2+}, Co^{2+}, Hg^{2+}, Fe^{3+}, Fe^{2+}, Zn^{2+}, F^-, CN^- etc (Colenda et al., 2018). The selectivity of indole-based chemosensors towards cations can be enhanced by introducing electron-rich species to the molecule. And also, it is influenced by the degree of the electron cloud in the ligand to be complexed with the metal ion (Ajaz A. Dar, 2018, Zhu et al., 2008).

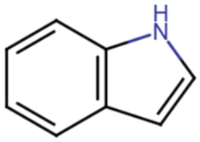

Figure 2. Chemical structure of indole

3. The sensing mechanism of Cu^{2+}

The fluorescence enhancement or fluorescence quenching process of synthesized ligands can be used to explain the sensing mechanism of Cu^{2+} ions. The Chelation Enhanced Fluorescence effect (CHEF) and the Chelation Enhancement Quenching effect (CHEQ) are affected by the enhancement of fluorescence emission and fluorescence quenching respectively. When compared to the unbound ligand, new absorption bands formed after complexation are typically important indicators that a complex has formed. The electron transition from the singlet excited state (S_1) to the singlet ground state (S_0) causes fluorescence in the receptor associated with filled metal ions. However, the Cu^{2+} undergoes a strong intersystem crossing from the singlet excited state (S_1) to the triplet excited state(T_1), which is bimolecular non-deactivated through a nonradiative process due to its paramagnetic nature. As a result, the fluorescence of these metal-bound receptors is quenched. Even though the paramagnetic Cu^{2+} ion is expected to cause fluorescence quenching, another method for increasing fluorescence has been described. This is because of the Photoinduced Electron Transfer (PET) mechanism. In a PET chemosensor, an electron can be transferred to an excited fluorophore receptor in the presence of high-energy non-bonding lone pair. On the other hand, The coordination of the Cu^{2+} ion effectively stops electron transfer resulting in turn-on fluorescence via PET inhibition (Suganya et al., 2018, Udhayakumari et al., 2017).

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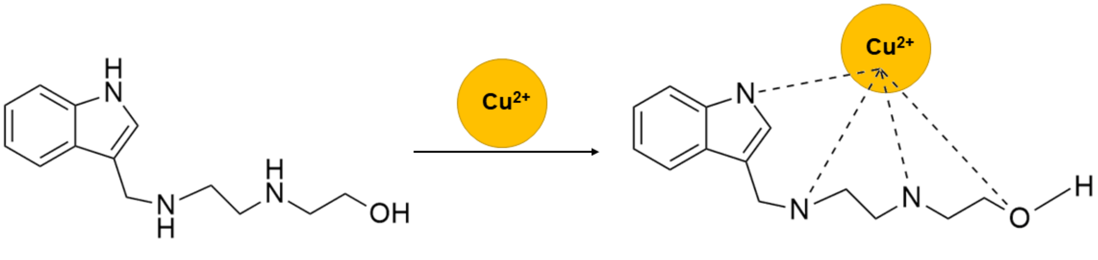
3.1. Sensor-based on the amino group and hydroxyl group as a recognition unit



1 **1-Cu^{2+}**

Figure 3. Feasible binding mode for probe 1 and Cu^{2+}.

Indole and its derivatives play a critical role in the formation of cation receptors. The nitrogen atom of the indole acts as an acceptor and a donor in metal-ligand binding.

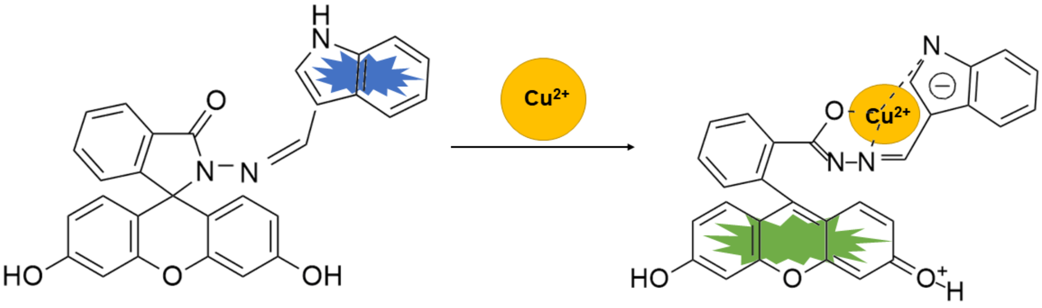
Indole-based chemosensor **1** was synthesized by Geng and co-workers for the qualitative and quantitative detection of Cu^{2+} ions in ethanol (Figure 3) (Huamei Geng, 2011). Chemosensor **1** demonstrated high selectivity and sensitivity towards Cu^{2+} ions over other metal cations such as K^{+}, Na^{+}, Ca^{2+}, Cr^{2+}, and Mg^{2+}. Nitrogen atoms and one oxygen atom in sensor **1** take part in the complex formation between probe **1** and Cu^{2+} resulting in the development of the host-guest complex. In comparison to the other metal cations, the addition of Cu^{2+} ions significantly quenches the fluorescence intensity due to the paramagnetism of Cu^{2+}. Furthermore, the paramagnetic cupric ion always favors the formation of complexes with square planar geometry (Dong et al., 2009). As a result, the fluorescence intensity was decreased showing that Cu^{2+} complexation with the one oxygen atom and three nitrogen atoms in **1**-Cu^{2+}.

The probe **1**-Cu^{2+} effectively quenches the emission intensity due to the transfer of electrons between the transition metal and the activated fluorophore (Muthuraj et al., 2014). When the concentration of Cu^{2+} was increased, the fluorescence emission spectra moved to a shorter wavelength, from 349 nm to 338 nm, and the fluorescence intensity also significantly decreased. The intra-ligand transitions of the indole moiety are responsible for the blue shift of this chemosensor (Zhou and Yang, 2006). The Benesi-Hildebrand study confirms that the stoichiometry of the **1**-Cu^{2+} complex was estimated to be 1:1 and the limit of detection was found to be 10^{-7} M.

3.2 Sensor-based on fluorescein-indole as a recognition unit

Fluorescein is a biologically compatible fluorophore with a high molar extinction coefficient, good water solubility, and strong fluorescence quantum yield. Fluorescein is also employed as a core component in a variety of fluorescent probes.

Muthuraj and co-workers reported a biocompatible indole-3-carboxaldehyde functionalized fluorescein hydrazone (FI) based "turn-on" chemosensor **2** to recognize Cu^{2+} ions selectively (Figure 4) (Muthuraj et al., 2014). The Cu^{2+} induces intramolecular transfer of fluorescence resonance energy (FRET) between the donor (indole-3-carboxaldehyde) and the acceptor fluorophore (xanthene). The absorbance maxima in a solution of FI (50 μM) in 10 mM HEPES (pH 7.4) buffer exhibited at 340 nm that is corresponding to the indole moiety. New absorbance bands at 492 nm and 620 nm appeared when Cu^{2+} is added to FI, showing that the xanthene group is in the open spirolactam ring state. The open spirolactam ring state allows for naked-eye detection by signifying the color variation and intensification of emissions. The reported binding constant for the **2**-Cu^{2+} was estimated to be 1.19×10^4 M^{-1} corresponding to the Benesi-Hildebrand plot and the detection limit was found to be 22.2 nM (Kumar et al., 2013). In addition, a colorimetric response of the sensor with Cu^{2+} was observed using the fluorescein-indole paper strip. At pH 7.4, absorption was seen in the UV-vis spectrum at 492 nm and 620 nm, and the sensor (FI) changed color from light blue to bright green.



2

2-Cu^{2+}

Figure 4. Possible complex formation between 2 and Cu^{2+} (Muthuraj et al., 2014).

3.3 Sensor-based on bis-triazolyl as a recognition unit

The triazole moiety plays an important role in cation identification. Bis-triazolyl frameworks are excellent chelation sites for several heavy metals with a quenched fluorescence.

The Shi research group developed four bis-triazolyl indoleamine derivatives that are based on the "click ligation" of indoleamine with a bis-triazolyl moiety to detect Cu^{2+} selectively (Figure 5) (Shi et al., 2013). The Cu(I)-catalyzed azide-alkyne cycloaddition process (Cue-AAC) (Wang and Hawker, 2011) is an excellent chemical ligation technique for making functional compounds that have been used to synthesize certain triazole-containing chemosensors (Deng et al., 2012a, Deng et al., 2012c, Deng et al., 2012b). The Cue-AAC compounds exhibited a severely quenched fluorescence in the presence of Cu^{2+} with a rapid color change over a wide range of metal cations. The bis-triazolyl moiety in the synthesized compounds acts as a receptor for Cu^{2+}. In addition, indole moiety for F^- exerts specific and reversible fluorescence changes along with colorimetric alternations upon the ligand–ion recognitions. The shift in color from yellow to green in probe **3** was associated with the fluorometric and colorimetric response of the ligand to Cu^{2+} upon interaction with it.

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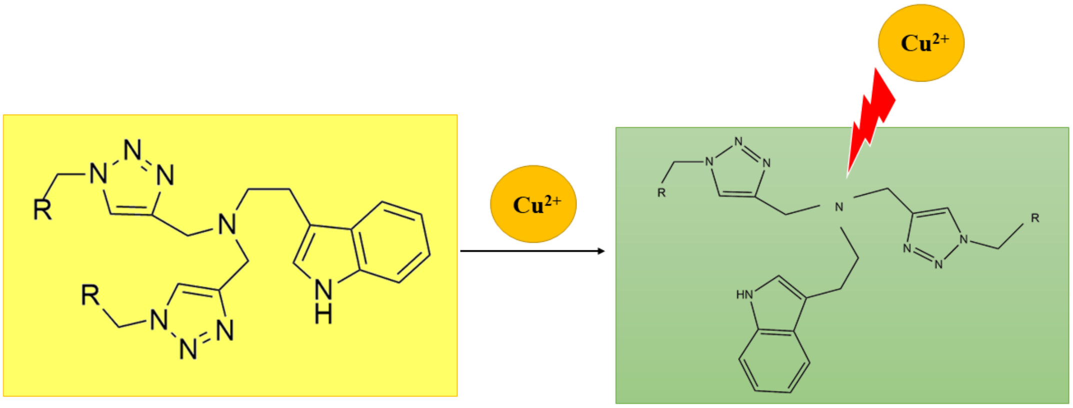
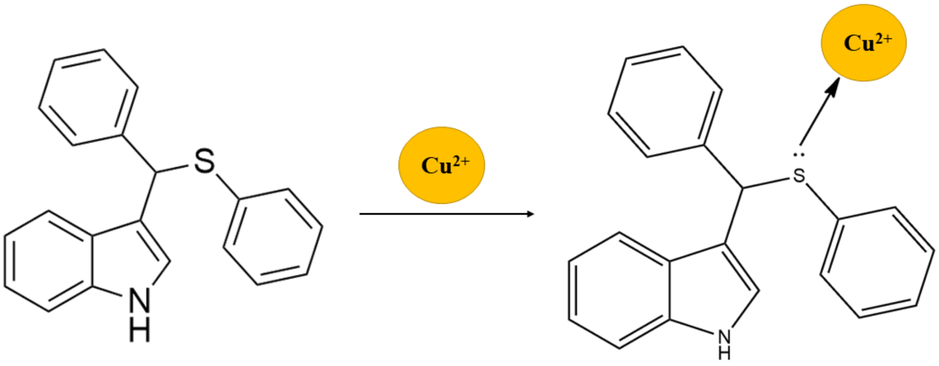


3 **3-Cu^{2+}**

Figure 5. Mechanism of Cu^{2+} sensing using 3 and its complex (Shi et al., 2013).

Jobs plot showed a 2:1 binding ratio between chemosensor 3 and Cu^{2+}. The addition of Cu^{2+} significantly quenches the fluorescence intensity owing to the transfer of electrons from the fluorophore to the receptor-Cu^{2+} region. This can be attributed due to the reversible "on-off" photoinduced electron transfer(PET) process (De Silva et al., 1997).

3.4 Sensor-based on benzenethiol as a recognition unit



4 **4-Cu^{2+}**

Figure 6. Binding mechanism of chemosensor 4 and Cu^{2+}.

In 2018, Dar and co-workers described the synthesis of 3-(phenyl(phenylthio)methyl)-1H-indole (Dar et al., 2014), chemosensor **4** which exhibited high selectivity towards Cu^{2+} in CH_3CN/H_2O (9:1) (Figure 6) (Dar et al., 2018). The introduction of Cu^{2+} ions leads to a significant rise in fluorescence, while the fluorescence intensity remained largely unchanged upon the addition of other alkali or transition metal ions. Furthermore, the above alkali and transition metal ions didn't show a fluorescence intensity increment even at a concentration of 50 μm. However, when the concentration of Cu^{2+} ions has been increased, it produces an improvement in fluorescence intensity with the appearance of a new emission band at 338 nm. The Sulphur in benzenethiol takes part in the complexation formation between chemosensor **4** and Cu^{2+} cation because the addition of electron-donating groups to an indole-based framework can reduce the anions' affinity (Wang et al., 2011). Job's plot demonstrated that the chemosensor **4** and Cu^{2+} had a 1:1 binding stoichiometry.

According to the Benesi-Hildebrand expression, the association constant for **4** with Cu^{2+} was 0.05 M^{-1} and formed 1:1 stoichiometry indicating a good tally with Job's plot. Moreover, this study indicated that an indole-derived chemosensor has been employed as a "turn-on" fluorometric probe for Cu^{2+} ions with a high detection limit of 108 nm in CH_3CN/H_2O (9:1) media.

3.5 Sensor-based on thiourea as a recognition unit

Thiourea-based cation receptors have gained a lot of expertise in the context of cation coordination chemistry and sensing.

Chemosensor **5**, which is based on *N*-Phenylthiosemicarbazones, was synthesized by the Shi group and used for the selective detection of Cu^{2+} (Figure 7). The rise in fluorescence intensity observed in probe **5** is attributed to a photoinduced electron transfer (PET) mechanism as described by (Udhayakumari et al., 2014). When interacting with Cu^{2+}, the color of chemosensor **5** changes from colorless to green due to the deprotonation of the receptor, initiating a complexation involving a nitrogen and a sulfur atom with Cu^{2+}. Furthermore, the initially colorless solution of chemosensor **5** turns violet in the presence of Cu^{2+}, indicating its selective detection of Cu^{2+} ions over other interfering metal ions. It indicates the fact that stability of Cu^{2+} ions in the availability of the other cations in the medium.

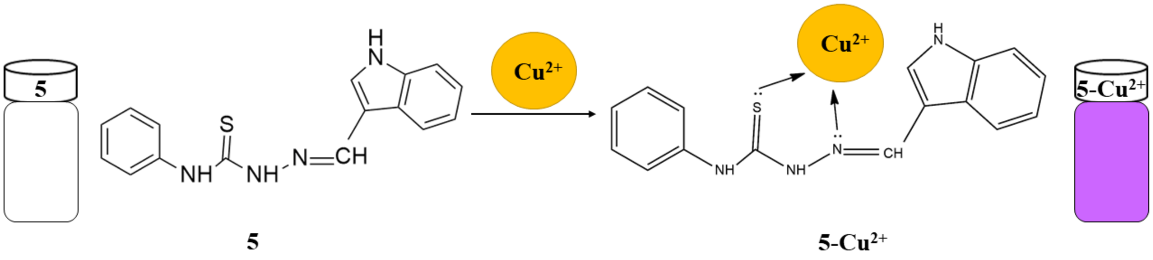
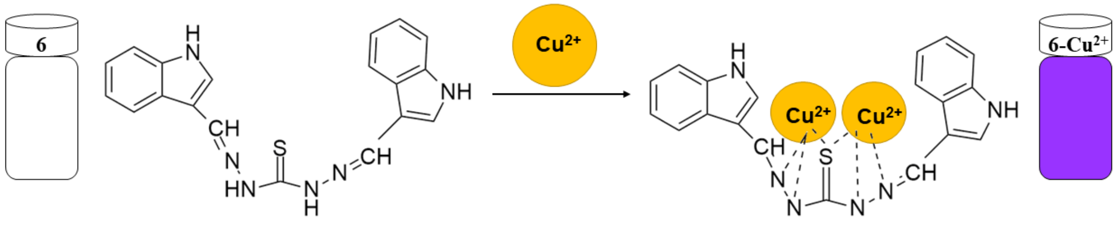


Figure 7. Feasible binding mode for 5 and Cu^{2+} (Udhayakumari et al., 2014).

In this experiment, the binding nature of probe **5** was examined under UV–vis spectroscopy. The addition of Cu^{2+} produces a large bathochromic shift at 330 nm– 340 nm peak in CH_3CN. Furthermore, the emission spectra of sensor **5** with metal cations were studied to demonstrate the effectiveness of probe **5** as a fluorescence chemosensor for the sensing of Cu^{2+} ions. The addition of Cu^{2+} produces a considerable fluorescence enhancement along with a greater red shift at 450 nm. Benesi–Hildebrand plots indicated a 0.18×10^{-8} association constants and the Jobs plot showed a 1:1 binding ratio between chemosensor **5** and Cu^{2+}.

Schiff base fluorescent probe which is known as 1,5-bis(indole-3-carbaldehyde)thiocarbohydrazone (IHT) has been synthesized by Chang and a research group in 2020 for the selective detection of Cu^{2+} (Figure 8) (Chang et al., 2020). The alteration in the color of chemosensor **6** upon its interaction with Cu^{2+} ions was attributed to the Chelation-Enhanced Fluorescence (CHEF) and Internal Charge Transfer (ICT) mechanisms in MeCNTris-buffered aqueous solution.



6 6-Cu^{2+}

Figure 8. Possible complex formation between 6 and Cu^{2+} (Chang et al., 2020).

The unbound probe of 1,5-bis(indole-3-carbaldehyde)thiocarbohydrazone (IHT) had a mild fluorescence emission at 453 nm. The introduction of Cu^{2+} resulted in a notable increase in fluorescence intensity, unlike the other studied metal cations, which did not prompt significant fluorescence changes. Chemosensor **6** demonstrated high selectivity, serving as an activated fluorescent sensor specifically for Cu^{2+}. The enhancement in fluorescence intensity upon complexation with Cu^{2+} was facilitated through the CHEF and ICT mechanisms in sensor **6**. In this process, one nitrogen atom and one sulfur atom participate in the formation of the complex between IHT probe **6** and Cu^{2+}. Chemosensor **6** may show low fluorescence intensity due to its flexibility. However, the free rotation of probe **6** was limited due to the availability of the Cu^{2+} in the medium, and the generated **6**-Cu^{2+} complex became stiffer than the unbound probe as a result of the CHEF effect (Sinha et al., 2014). The fluorescence intensity of the **6**-Cu^{2+} was enhanced with the increasing concentration of Cu^{2+} ion, reaching a maximum with a redshift of 7 nm from 441 nm to 448 nm. Afterward, the fluorescence intensity has almost remained constant at greater Cu^{2+} ion concentration. Jobs plot experiment gives 1:2 binding stoichiometry between probe **6** and Cu^{2+} and the limit of detection towards Cu^{2+} was found to be 8.93×10^{-8} M (Dai et al., 2018). This study indicated that the probe IHT might be used as a sensitive probe for the detection of Cu^{2+} ions in aqueous environments.

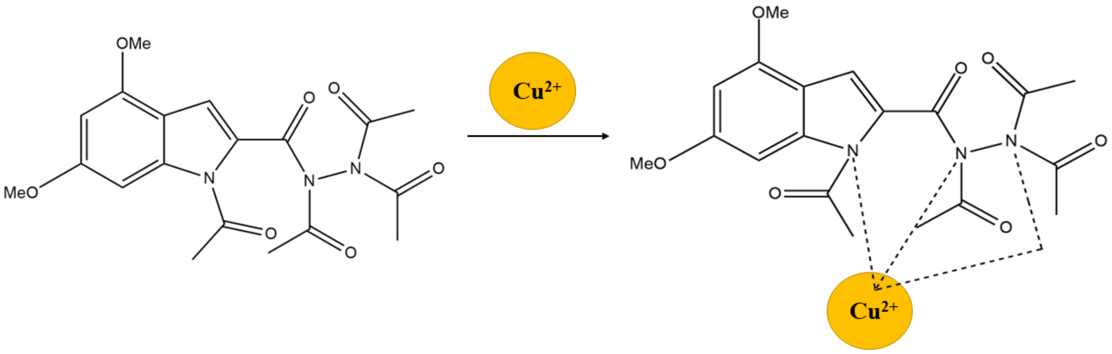
3.6 Sensor-based on 4,6-dimethoxyindole-2-carbohydrazide as a recognition unit

In 2019, Şenkuytu and co-workers reported the synthesis of a 4,6-dimethoxyindole scaffold-based fluorescent chemosensor **7** with no interference from other competing metal ions (Figure 9) (Şenkuytu et al., 2019). The substitution of four NH functional groups with N-COCH$_3$ in 4,6-dimethoxyindole-2-carbohydrazide had a significant impact on the selectivity and sensitivity towards the detection of Cu^{2+} ions. Different organic solvents, including acetonitrile, dichloromethane, tetrahydrofuran/water, tetrahydrofuran, dimethylsulfoxide/water, dimethylsulfoxide, and chloroform, were used to analyze the photophysical performance of chemosensor **7**. The absorbance bands of the compounds did not alter, despite the solvent impact on their absorbance intensity. In tetrahydrofuran and dimethyl sulfoxide solvents, a bathochromic shift at 14 nm was observed and it was within the fluorescence emission wavelength of receptor **7**. This occurs due to the formation of non-covalent intermolecular forces between receptor **7** and solvents. As Cu^{2+} ions were introduced, metal-ligand charge transfer (MLCT) transitions between Cu^{2+} ions and the oxygen atoms of sensor **7** were shown to increase absorbance at 298nm and 345nm (Maamar et al., 2009). Moreover, the introduction of Cu^{2+} induces a pronounced quenching effect.

The limit of detection towards Cu^{2+} was found to be 10.30 µM and hence this study suggests that the 6-dimethoxyindole scaffold-based sensor showed a low detection limit and thus a strong selectivity for the copper (II) ions.

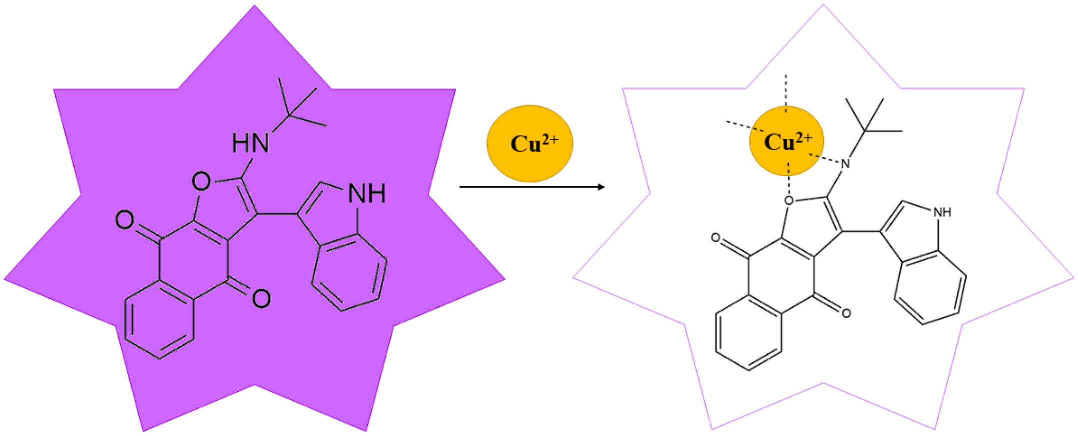
3.7 Sensor-based on indoylfuranone as a recognition unit

Indoylfuranone-based bifunctional turn-on fluorescent and turn-off colorimetric chemosensor **8** was reported by the Sharma group (Figure 10) (Kumawat et al., 2016). Chemosensor **8** behaves as a unique turn-off colorimetric bifunctional chemical sensor that detects copper(II) ions selectively in both aqueous and semi-aqueous phases (Hu et al., 2014, Kim et al., 2015). Moreover, the Furadione solution showed a rapid and noticeable change of color from dark purple to colorless with the presence of an equimolar quantity of Cu^{2+} ions



7 **7-Cu^{2+}**

Figure 9. Binding mechanism of chemosensor 7 and Cu^{2+}.



8 **8-Cu^{2+}**

Figure 10. Visual fluorescence response of sensor 8 towards Cu^{2+} (Kumawat et al., 2016)

However, the presence of an equimolar quantity of cupric ions drastically lowered the absorbance intensity at 574 nm wavelength. Moreover, it causes a significant reduction of

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fluorescence intensity of cupric ions with a dramatic color change. Chemosensor **8** shows excellent selectivity towards Cu^{2+} with no interference from other competing metal ions.

The association constant of sensor **8** (6.94×10^{4} M^{-1}) suggests that the indoylfuranone-based chemical probe **8** has a greater affinity for Cu^{2+} with the complexation with a nitrogen atom and an oxygen atom in indoylfuranone. Job plot analysis indicated a 1:1 binding ratio of the complex. In addition, the quantification limit for the **8**-Cu^{2+} complex was calculated to be 3.18×10^{-7} M.

3.8 Sensor-based on carbohydrazide with dansyl chloride as a recognition unit

Chemosensor **9**, which is based on the reaction between 1H-indole-2-carbohydrazide with dansyl chloride**,** was synthesized by the Sie research group for the selective detection of Cu^{2+} ions (Figure 11). The addition of Cu^{2+} produces an increase in the fluorescence in CH_3CN/H_2O (v/v,9:1) medium (Sie et al., 2018). Indole and dansyl chloride were coupled as a donor-receptor couple for the transfer of fluorescence resonance energy (FRET) in probe **9**. The bright yellow color solution of chemosensor **9** becomes dark blue in the presence of Cu^{2+} ion along with a red shift at 290 nm.

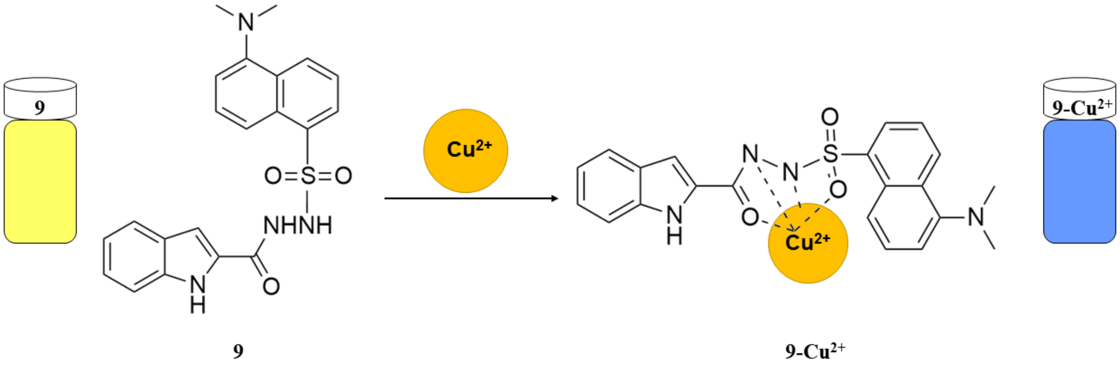

Figure 11. Possible binding method of 9 and Cu^{2+} (Sie et al., 2018).

The introduction of Cu^{2+} results in an increase in fluorescence intensity with a shift toward shorter wavelengths. Moreover, the association constant of the 9-Cu^{2+} complex in a CH_3CN/H_2O (v/v, 9:1) solution was estimated to be 5.3×10^{8} M^{-2}. Jobs plot analysis revealed a binding ratio of 1:2 between 9 and Cu^{2+}.This study demonstrated that probe **9** was a very selective and sensitive sensor for the detection of Cu^{2+} ions and also this produced a turn-on, fluorescence ratiometric signal.

3.9 Sensor-based on NOR and YES logic functionalities as a recognition unit

N-alkylindole-based "ratiometric" and "turn-off" chemosensor **10** , was synthesized by the Kaur group using a condensation reaction. Chemosensor **10** showed a contrasting fluorescence response towards Cu^{2+} ions with NOR and YES logic functionalities (Kaur et al., 2011). Chemosensor **10** acts like a fluorescent molecular switch when Cu^{2+} is present. The absorbance spectrum of sensor **10** was altered in nearlyidentical ways by the incremental addition of Cu^{2+}. The

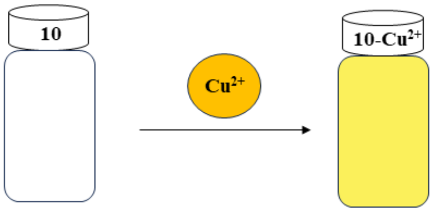

Figure 12. Color change due to the complexation formation between 10 and Cu^{2+}.

low energy peak that caused the color shift from colorless to yellow (Figure 12) occurred at 476 nm.

Job's plot analysis revealed that probe **10** and Cu^{2+} showed 1:1 binding stoichiometry. The binding constant was calculated to be 4.85 and the limit of detection and predicted limit of quantification was found to be 1.67×10^{-6} M and 1.2×10^{-7} M respectively (Gans et al., 1996). The existence of Cu^{2+} ions resulted in a 'turn-off' signal in the medium due to the paramagnetic property of the Cu^{2+} ion.

4. Conclusion and future perspectives

In this review, we focused on developing chemosensors that could detect the Cu^{2+} ion selectively using a specific type of fluorescent and colorimetric probe with an indole functional group, which have become powerful tools in analytical and supramolecular chemistry. This review summarizes the recent publications on indole-based colorimetric and fluorescent chemosensors for the selective detection of Cu^{2+} ions. According to their receptors, there were numerous different types of fluorescent and colorimetric chemosensors, each with specific functional groups or features. They are as an amino group and a hydroxyl group, fluorescein-indole, bis-triazolyl, benzenethiol, thiourea, 4,6-dimethoxyindole-2-carbohydrazide, indoylfuranone, carbohydrazide with dansyl chloride, and NOR and YES logic functionalities. For the aforementioned categories, a summary of the interactions with the Cu^{2+} ions and the sensing processes was provided. Interestingly, certain Cu^{2+} probes exhibit fluorescence increases due to suppression of the photoinduced electron transfer (PET) process, while others exhibit fluorescence quenching due to the paramagnetic character of the photoinduced electron transfer mechanism (PET). In the presence of Cu^{2+} ions, the majority of the described chemosensors demonstrated a dramatic and rapid color change. Furthermore, the indole-based compounds were also used to create fluorescence and colorimetric chemosensors with turn-on and turn-off ratiometric responses.However, the majority of the chemosensors evaluated in the current literature detect copper ions in organic solvents, restricting their application. As a result, more study is needed to construct innovative supramolecular assemblies, solid films, and supramolecular gels employing indole-based derivatives to detect Cu^{2+} ions in an aqueous medium. In addition, only a few chemosensors with reversible features have been identified, which is a drawback in this sort of host-guest chemistry. Therefore, it is crucial to consider whether recycling these resources is necessary in order to limit waste formation. Furthermore, designing and synthesizing a total water-soluble effective indole-based chemosensor for Cu^{2+} detection remains a difficult challenge. The introduction of a polar functional group aids the chemosensor in becoming soluble in water and therefore useful in application. This study will most likely lead to new directions in the development of indole-based chemosensors for Cu^{2+} ions as well as other environmental and biological analytes.

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