

Systematic Review

# Investigating the Potential of 8-Amidoquinoline Derivatives as a Fluorescent Probe for Zinc Detection: A Systematic Literature Review

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**Abstract:** Abundant of preparatory works have recognized that fluorescent sensors based on 8-aminoquinoline are popular tools to detect Zn<sup>2+</sup> ions in environmental and biological applications. Along with these studies, researchers started to introduce a variety of carboxamido group into an 8-aminoquinoline molecule in forming 8-amidoquinoline derivatives. Therefore, this systematic review aims to introduce a general overview of the fluorophore 8-aminoquinoline as Zn<sup>2+</sup> receptors and to provide comparisons of collected studies that related to 8-amidoquinoline derivatives as fluorophore probe of the sensor. According to PRISMA systematic searches strategy, 13 articles were analyzed for trends, research designs, results and discussion, subject samples, and remarks or conclusions. We found cross-sectional studies with four aspects in zinc sensing that have been targeted; binding studies via titration, detection's limit, interferences studies, and validation of the study. Hence, this paper also included assessments of those criteria and the trends of development of 8-amidoquinoline derivatives based-zinc fluorescent chemosensor. It also showed that most of the researches conducted in China. In conclusion, this study identified various research designs of fluorescent chemosensors based on 8-amidoquinoline prolong with the effectiveness and potential as a recognition probe to assist the detection of zinc. Hence, elucidation of those derivatives essential to be explored because more studies are needed to improve the sensing criteria of the zinc sensor.

**Keywords:** Zinc sensor; 8-amidoquinoline; Fluorescent probe; Chemosensor; Systematic review

## 1.0 Introduction

Chemical sensors, or known as chemosensors, are devices that are used for sensing target compounds by converting chemical information into "analytical" information. These analytical terms will imply the notion of measurability, whether in the qualitative or quantitative form [1]. Molecular recognition of chemosensor involves incorporating a chromophore or fluorophore as a binding site for analyte and consists of a mechanism of interactions between them [2,3]. Therefore, chemosensors have been playing an essential role in detecting various analyte in many diverse fields, especially in analytical chemistry, bio- medicinal science, and environmental chemistry[4–9]. There are various types of chemosensor, including fluorescent sensors using spectrophotometry and fluorimeter to detect analytes [10–19].

Development of simple design and easy to synthesize fluorescent sensors with high selectivity recognizing metal ion is widely studied for its promising advantages. As ion-induced sensors, a fluorescent probe is highly useful for various applications such as in vivo and in vitro analyses of biologically essential species, including metal ions. It offers many advantages over other techniques because of its high sensitivity, selectivity, instantaneous response besides offering instrument less detection [20]. Despite the progress of fluorescent chemosensors in various detection, several problems and challenges continue to have existed lead to an exploration of the development of binding receptors.

The past decade has seen many excellent metal-ion sensors been reported to detect transition and heavy metal ions such as zinc ions  $Zn^{2+}$ .  $Zn^{2+}$ , as an essential element in the human body, is actively involved in various biochemical processes such as neuronal signal transmission, D.N.A. binding, enzyme regulators as well as catalytic centres.  $Zn^{2+}$  deficiency and imbalance distribution then lead towards a much broad range of pathologies in parts of body systems [21,22]. Considering that  $Zn^{2+}$  is spectroscopically silent due to its  $d^{10}$  electronic configuration, fluorescent chemosensors of Zn were extensively studied. That are so many receptors used as fluorophore as binding sites such as di-2-picolylamine (DPA) [23–25], quinoline [25–27], bipyridine[28–31], acyclic and cyclic polyamines [29,32,33], iminodiacetic acid [34–36], triazole [37–39], and Schiff-base receptors [40–42].

Quinoline is an exciting class of compound with low initial fluorescence but can form highly fluorescent complexes with metal ions was chosen as a fluorophore [43]. Derivatives of 8-hydroxyquinoline and 8-aminoquinoline are common fluorogenic chelators for  $Zn^{2+}$  ions [25]. Then, the derivatives of 8-aminoquinoline in the presence of amide gradually to be acknowledged. Several studies focusing on improving and increasing the sensitivity and selectivity of fluorescent probes for  $Zn^{2+}$  based on 8-amidoquinoline and its derivatives are widely developed [44,45]. 8-amidoquinoline derivatives exhibit fluorescence properties for sensing  $Zn^{2+}$  based on important signalling mechanisms, internal charge transfer (I.C.T.) [45,46].

Therefore, this review aims to provide assessments of collected studies that related to 8-amidoquinoline derivatives as fluorophore of zinc chemosensor and help in elucidating molecular receptors in a reachable way to those who enter the field. The systematic searching and screening regarding that matter are done according to PRISMA guidelines [47].

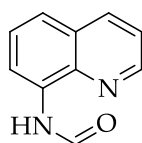
## 2.0 Methods

### 2.1 Search strategy

The following electronic database was searched through the medium of PubMed, ScienceDirect, Scopus, and Web of Science (all published between 2010 until January 2020). The search strategy involved the following keywords; "8-aminoquinoline", "quinoline-8-amine," and "detection of zinc." So we started the search by searching those keywords in the chosen database. The search begins with "8-aminoquinoline" OR/AND "detection of zinc" and continue with another name of "quinoline-8-amine" OR/AND "detection of zinc." We found nothing related to quinoline-8-amine due to the probability of the use of common names among researchers.

### 2.2 Inclusion and exclusion criteria

All articles were limited only to the studies published in the English language. Further on, only primary kinds of literature on 8-aminoquinoline with amide structure known as 8-amidoquinoline or N-(quinolin-8-yl)formamide (Figure 1) as a fluorescent probe for zinc detection were included. Proceedings, letters, news, editorials, or case studies were excluded from this study.



**Figure 1.** Structure of 8-amidoquinoline or N-(quinolin-8-yl) formamide

### 2.3 Data extraction and management

Two reviewers (NSM, NHZ) independently screened the articles before their inclusion, which includes the article's titles, keywords abstracts, or full text to ensure inclusion and exclusion criteria adhered. Any disagreement was resolved by discussion, and the remaining papers were read thoroughly before all the data were extracted. The following data were recorded from the studies: aims of the study, methods; result and discussion; subject samples; and remarks or conclusion.

## 3.0 Results and discussion

### 3.1 Fluorescent Zn chemosensor based on 8-aminoquinoline

A fluorescent chemosensor signal is typically calculated as changes of fluorescence intensity and/or transition of fluorescence wavelength, especially before and after introducing probe to the target [25]. Until now, this fluorescence activity that involves cations and anions has been enabled by several mechanisms, such as internal charge transfer (I.C.T.), chelation enhanced fluorescence (CHEF), photoinduced electron transfer (P.E.T.), and deprotonation mechanism [48]. By these mechanisms, the fluorescence intensity of the chemosensor could be quenched or enhanced depends on the probe. Several compounds had been studied along with the mechanism involved to get a better understanding of fluorescent chemosensors.

However, it is necessary to notice that few compounds fluoresce by itself or fluoresce after the interaction with the target. The behaviour of the compounds usually can electronically go to excited and ground state during inter-intramolecular transfer. Thus, the most intense and valuable fluorescence is generally seen in compounds that comprise aromatic functional groups, since they have a  $\pi$  system orbital [49]. Therefore, earliest probes for zinc (II) detection are derivatives of zinquin [50], Zinbo-5 [51], Zinpyr [52], aminoquinoline [53] and coumarin families [54].

It is crucial to keep in mind that fluorescent groups that have lone pairs of electrons like nitrogen will be quenching the emission. However, the coordinate bond formed between that lone pairs of electrons and metal ions like  $Zn^{2+}$  ion can prevent fluorescence from quenching. Hence, those nitrogen-containing heterocyclic chromophores whose nitrogen will form a ring of chelate with metal ions that will give an enhanced fluorescence (CHEF) effect [49]. Upon excitation, the electron donor from the chelator to the acceptor will permit intramolecular charge transfer (I.C.T.), preceded by a large Stokes' shift [48]. This chemosensor design would be valued as a wavelength-shifted fluorescence intensity enhancement that will further amplify the recognition event. Therefore, 8-aminoquinoline started to get knowledge as selective derivatives for zinc detection.

An aryl sulfonamide derivative of 8-aminoquinoline, 6-methoxy-(8-p-toluenesulfonamido)quinoline (TSQ) is amongst the most efficient used as fluorophore in zinc sensor, especially in the biological field. This TSQ was first published in the early seventies by Toroptsey and Eshchenko

[55]. Then, conferring to [56], TSQ act as a chelating ligand to  $Zn^{2+}$  by ratio 2 to 1 ((TSQ)<sub>2</sub>Zn) which will be formed metal complex. TSQ-Zn will increase the fluorescence intensity of TSQ by 4-folds (excitation maximum: 360 nm, emission maximum: 490 nm). They also indicate a blue-shifted emission spectrum as a signal of the formation of ternary TSQ-Zn-protein adduct.

TSQ derivatives are extensively used as fluorogenic chelators in the detection of zinc in the biological samples. However, these derivatives are low water solubility, poor in membrane penetrability, and complicating the measuring of free zinc ion in cell quantitatively [48]. Therefore, to overcome those problems, 8-carboxamidoquinoline derivatives started to get attention as receptors to detect  $Zn^{2+}$  ion, especially in biological fields.

The carboxamido group is deprotonated after  $Zn^{2+}$  binding, and the 8-aminoquinoline intramolecular hydrogen bond is broken to inhibit the electron-transfer process, which quenches the fluorescence of quinoline [57]. Xie and co-workers (2012) also reported this carboxamidoquinoline affords two coordination sites for  $Zn^{2+}$  ion to bind [58]. Aside from these two sites, the introduction of a 2-(2-hydroxyethoxy)-ethylamino group recorded an 8-fold rise in quantum fluorescence yield and a red-shift of 75 nm in fluorescence emission when  $Zn^{2+}$  was bound in aqueous buffer solution.

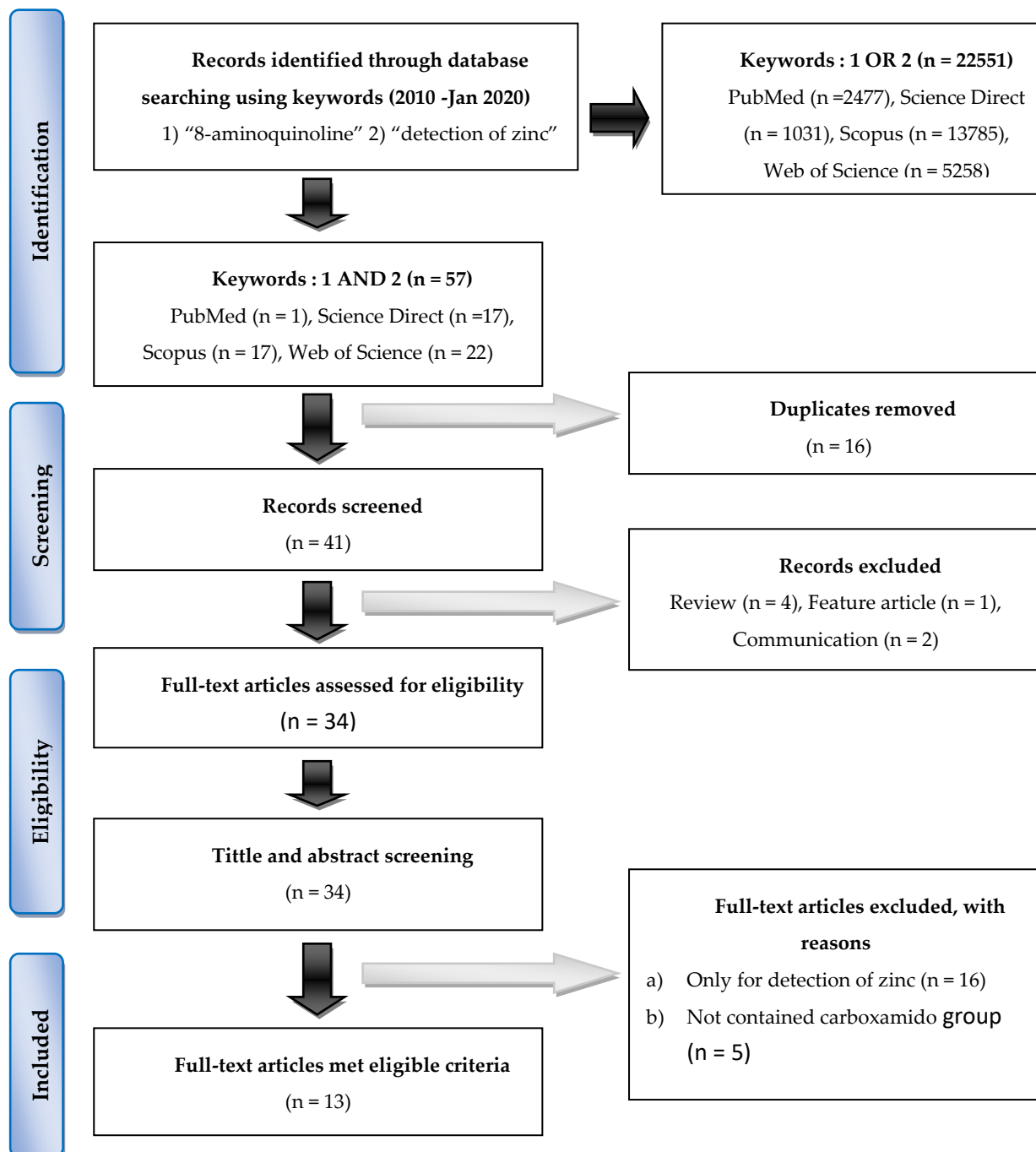
A research study by [59] demonstrated the binding complex formation between  $Zn^{2+}$  and receptors are versatile. It depended on the receptor itself and the environment of the binding. They proved three different receptors (Q.P., NA, QA) gave different coordination upon binding with  $Zn^{2+}$  even though all the receptors were almost similar, which contained 8-carboxamidoquinoline and dipicolylamine (D.P.A.). Generally,  $Zn^{2+}$  favoured nitrogen of quinoline and nitrogen or oxygen from the amide group and of course nitrogen from D.P.A. These results proved to add an amide group into 8-aminoquinoline as a better decision in improving the chemosensor of Zn(II). As mention before, aside increase water solubility and membrane permeability, the amide group also helps the sensor to be more selective and efficient by growing the tendency of the binding.

Therefore, this systematic search is needed to get a better understanding on the development of 8-carboxamidoquinoline as receptors of Zn(II) sensor with all due respect to enhanced sensitivity and selectivity for future studies, especially in the biological application. The result of the interaction and coordination of  $Zn^{2+}$  with existed 8-carboxamidoquinoline derivatives differed, thus many factors required to be considered.

### 3.2 Data extraction result from systematic searches

As stated above, we succeed in narrowing down several relevant articles by using systematic searches in PubMed, ScienceDirect, Scopus, and Web of Science database. Those 57 articles encountered the standard based searching by using two keywords 1) "8-aminoquinoline" AND 2) "detection of zinc" in the article's titles, keywords, abstracts, or full texts. In total, 41 titles and abstracts were screened by authors independently based on criteria "practices of 8-aminoquinoline derivatives in the detection of zinc only". Next, the left articles were evaluated for inclusion or exclusion based on 8-aminoquinoline with amide structure, or we might be called it 8-amidoquinoline or N-(quinolin-8-yl) formamide (Figure 1). The addition of the carboxamido group and then the breaking of the intramolecular hydrogen bond of 8-aminoquinoline, which will inhibit intramolecular electron-transfer, in turn, enhance the I.C.T. process as pronounced in the Liangwei Zhang [60] and Zhaochao Xu [61] report, these would enhanced fluorescence emission.

As a conclusion of systematic searching, the search generated 57 articles, of which only 13 articles fulfilled the inclusion criteria. Figure 2 shows the flow chart of the selection procedures in identifying qualified articles for the review. Then all data were extracted directly from the final articles that met eligible criteria. Further details on each article regarding research design and outcomes were summarized in Table 1.



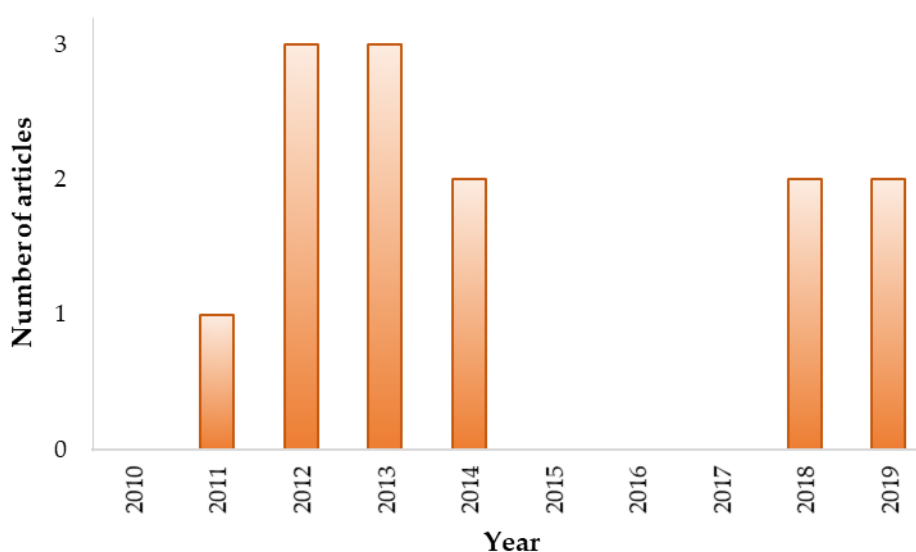
**Figure 2.** Flow chart of searching results and screening strategy according to PRISMA guidelines.

1 **Table 1.** The comparisons and assessments of collected studies that related to 8-amidoquinoline derivatives as fluorophore of zinc chemosensor

Articles	Year	University/Countries	Probe	Binding Mode (Probe: Zn)	Interferences	Detection limits	Real sample
[62]	2013	Lanzhou University, China	PMQA	2:1	Cd <sup>2+</sup> , Co <sup>2+</sup> , Cu <sup>2+</sup>	8.85 × 10 <sup>-8</sup> M	HELA cells
[63]	2019	Shenzhen University, China	QLNPY	-	Cu <sup>2+</sup>	3.8 × 10 <sup>-8</sup> M	HepG2 cells
[60]	2012	Lanzhou University, China	Probe 1	1:1	Hg <sup>2+</sup> , Cu <sup>2+</sup> , Cr <sup>3+</sup> , Ag <sup>2+</sup>	8.14 × 10 <sup>-8</sup> M	HELA cells
[64]	2014	Nanjing Normal University, China	QA	1: 1	Hg <sup>2+</sup> , Cu <sup>2+</sup>	3.36 × 10 <sup>-8</sup> M	Intracellular cells
[59]	2013	Korea	QP	-	Cu <sup>2+</sup> , Fe <sup>2+</sup> , and Co <sup>2+</sup>	-	-
[65]	2019	Xi'an Jiaotong University, China	Probe 1	1:1	Cr <sup>3+</sup>	6.3 × 10 <sup>-8</sup> M	Tapwater
[43]	2018	Thailand	1	1:1	Ni <sup>2+</sup> , Cu <sup>2+</sup> , Co <sup>2+</sup>	160 × 10 <sup>-8</sup> M	Cabbage
[66]	2018	Zhoukou University, China	AQZ-2COOH	-	Cu <sup>2+</sup>	10.2 × 10 <sup>-8</sup> M	HeLa cells
[20]	2013	Xinxiang University, China	HAQT	1: 1	Ni <sup>2+</sup> , Cu <sup>2+</sup>	25.6 × 10 <sup>-8</sup> M	River water
[67]	2014	Jilin University, China	CuInS <sub>2</sub> QDs/8-aminoquinoline	1:1	Pb <sup>2+</sup> , Hg <sup>2+</sup>	445 × 10 <sup>-8</sup> M	Tap water
[51]	2012	The Chinese University of Hong Kong, China	Q.P.A.	-	Cd <sup>2+</sup> , Fe <sup>2+</sup> , Cu <sup>2+</sup>	13 × 10 <sup>-8</sup> M	HK-1 cells
[58]	2012	Lanzhou University, China	L1	-	Cd <sup>2+</sup> , Ni <sup>2+</sup> , Cu <sup>2+</sup> , Hg <sup>2+</sup>	100 × 10 <sup>-8</sup> M	Human bladder cancer
[68]	2011	United States	QTEPA-SiNPs	-	Fe <sup>2+</sup> , Cu <sup>2+</sup> ,	10 × 10 <sup>-8</sup> M	Yeast cells

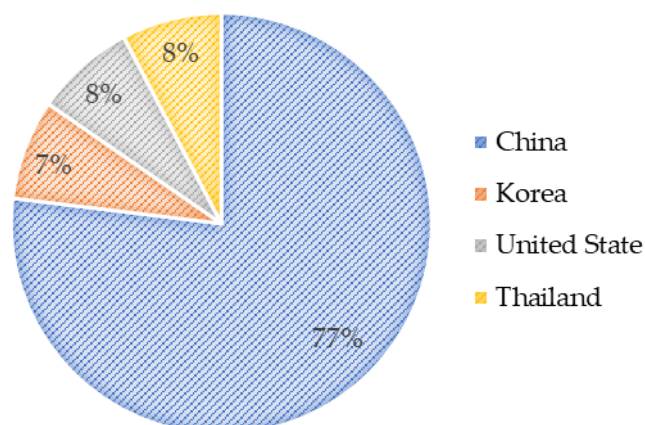
### 3.3 Results trends

The yearly publications distribution on 8-amidoquinoline as a fluorescent probe for zinc detection displays inconsistent trends (Figure 3). The number of studies noticeably increased from the year 2011 to 2012 and continue to be stagnant until 2013 before proceeding with decreasing publication in 2014. Then, there were no publications related to both keywords for three years. Nevertheless, then the studies started to be acknowledged again in 2018 and 2019. So, the authors assumed there would be extending research on the potential of 8-amidoquinoline derivatives as reagent to detect zinc in the following years. As we believed, this area of research would be shown an increasingly attracting academic's attention to cover more based on hard and soft acid and base (HSAB) theory.



**Figure 3.** Trends of publications on 8-amidoquinoline as a fluorescent probe for zinc detection per year.

The pie chart in Figure 4 showed percentages of the included publications among China (77%), United States (8%), Thailand (8%), and Korea (7%). In order to evade favoritisms on the highest percentage publications in China, the authors identify whether those studies were conducted by the same group or not. Only two articles were founded to be from the same group, while the other eight articles were from different universities in China (Table 1).



**Figure 4.** Percentages of the included publications among countries.



### 3.4 Research design and objectives

All the articles reviewed were cross-sectional studies with four sections - first, the function of synthesized 8-amidoquinoline derivatives as a recognition probe, second - titration analysis between probe and zinc ion (fluorescence titration or UV-Vis titration or both), third - the selectivity of the probe sensor with other competitive metal cations and finally, the limit of detection and reliability of the assessment according to the real sample applications. Most of the papers, starting with the synthesizing 8-amidoquinoline derivatives, then proceed with solution works that are involved titration of the compound with a zinc ion.

They continued with certain optimization before undergoes selectivity test with other transition metals such as cadmium ( $\text{Cd}^{2+}$ ), copper ( $\text{Cu}^{2+}$ ), cobalt ( $\text{Co}^{2+}$ ), nickel ( $\text{Ni}^{2+}$ ), chromium ( $\text{Cr}^{3+}$ ), silver ( $\text{Ag}^{2+}$ ), ferum ( $\text{Fe}^{2+}$ ), lead ( $\text{Pb}^{2+}$ ) and mercury ( $\text{Hg}^{2+}$ ). Latterly, they tested the sensor with real sample either from biological or environmental samples that involved requirement detection of zinc as per validation status. However, out of 13 articles, one research does not validate with real sample(s), only three articles tested with water, one article tested with cabbage, and the rest tested with biological samples (Table 1).

### 3.5 Criteria to evaluate the potential of 8-amidoquinoline derivatives as a fluorescent probe for zinc detection in each included articles

#### 3.5.1 Binding studies of 8-amidoquinoline probes via solution works

Most of the researchers started and trying to develop sensors specifically for the detection of zinc intensively. Among various conventional probes for zinc (II) are derivatives of zinquin [50], Zinbo-5 [51], Zinpyr [52], aminoquinoline [53] and coumarin families [54]. Meanwhile, 8-aminoquinoline and its derivatives [69] were among the first probes developed for zinc (II) detection. They exhibited excellent stability, high affinity to metal ions, and good membrane permeability [48]. However, this zinc (II) chemosensor developed had suffered to differentiate between zinc ion and other competitive cation metals such as  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ , and  $\text{Hg}^{2+}$  due to its  $3d^{10}$  electronic configurations (spectroscopically silent) [66,70].

An ideal chemosensor contains a receptor that has the most robust affinity binding towards Zn ion without interferences (signal-selectivity) of other heavy metals and has a broad linear responsive range that is highly explored. By inserting a functional group of amide into a conjugated molecule of 8-aminoquinoline,  $\text{Zn}^{2+}$  ion (borderline acid) is coordinated favourably with aromatic nitrogen atoms (borderline bases), N-amide, and O-amide. Based on this HSAB theory (hard and soft acids and bases), some researchers [71,72], including us, we are thinking of adding some more nitrogen and oxygen atoms into the 8-aminoquinoline molecule. We believed it could increase the binding affinity towards Zn(II) ion so that it will help to null out the competitive metals that have the same electronic configuration,  $3d^{10}$ .

In determining the binding studies between receptor 8-amidoquinoline compounds, all the papers reviewed were reported on characterization spectroscopy, fluorescence titration, and UV-Vis titration [20,43,73]. They seek for binding mode via job plot method and binding constant ( $K_d$ ) or association constant ( $K_a$ ). However, not all papers were recorded for job plot data. The binding modes were summarized in Table 1. Out of 13 papers, six of them do not do the job plot analysis. The left articles stated binding mode between probes and zinc ion was one to one ratio except for research studied by [62], (2:1).

The ligand added for 8-carboxamidoquinoline consisted of either nitrogen, oxygen, and/or sulphur due to existing of lone pairs of electron for each atom (Figure 4). These three atoms may react as electron-donating during the coordination binding with  $\text{Zn}^{2+}$ . However, as [74] mentioned since  $\text{Zn}^{2+}$  does not behave reliably either as a soft or as a hard Lewis acid, it poses a borderline case with no particular fondness for oxygen, nitrogen or sulfur-donor ligands to be coordinated, the results of the concluded binding coordination sites to form complexes were differ. Roughly, we



reviewed all of them as there were no fixed preferences and they differ based on derivative, atoms presenting, molecular geometry, medium, and environment. Therefore, the results might differ. Nevertheless, the importance of development in sensing  $Zn^{2+}$  was successful since the different enhancement for fluorescence upon binding with  $Zn^{2+}$  was recognized.

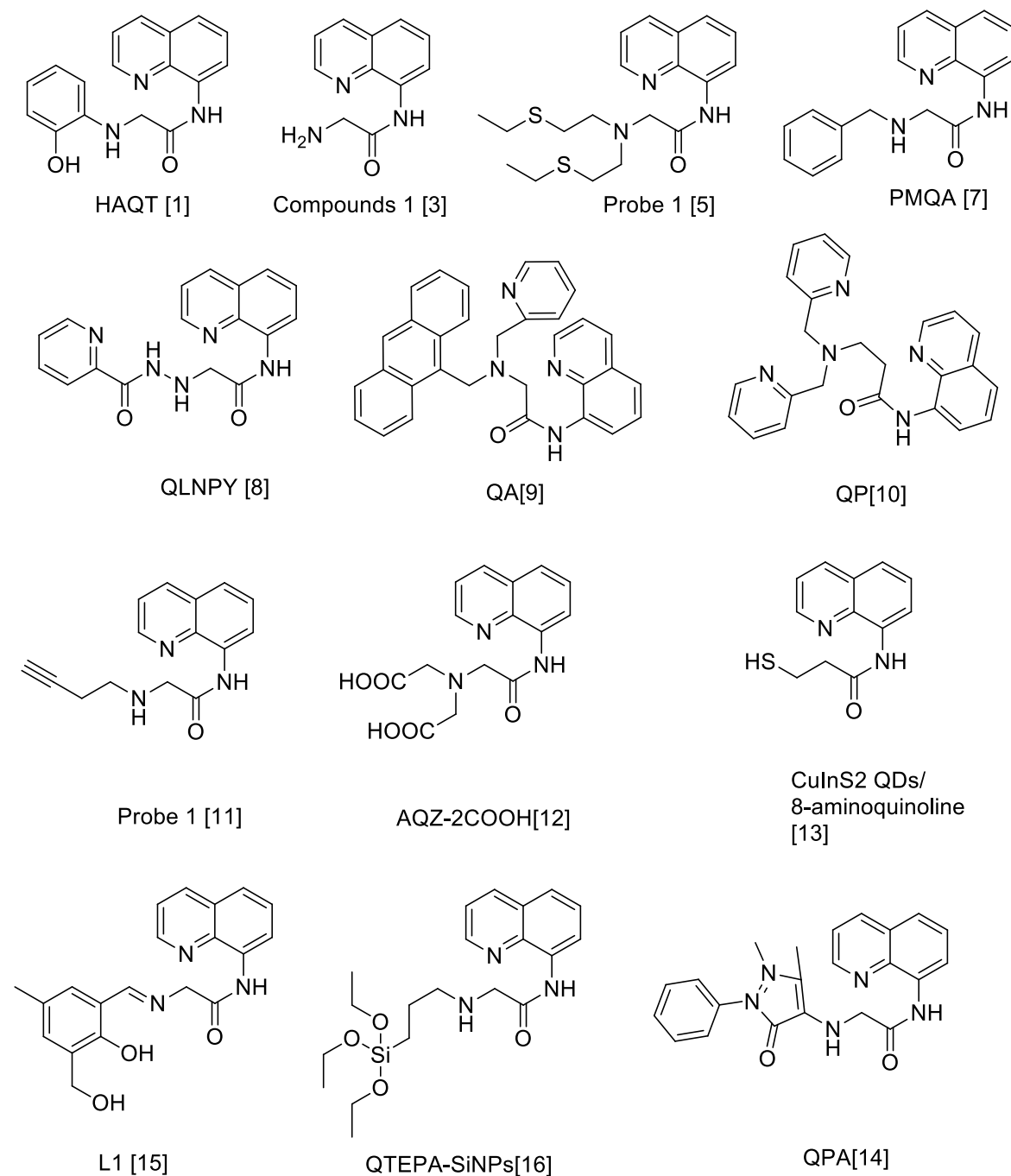


Figure 4 Chemical structures of 8-carboxamidoquinoline derivatives based on table 1

The delictants of Probe 1 was demonstrated good selectivity to differentiate between  $Zn^{2+}$  and  $Cd^{2+}$  through two tautomers; amide and imidic acid. The resonance of amide that was inserted into 8-aminoquinoline offered different binding modes and coordination complex. Therefore, the

fluorescence response signal varied according to the introduced metal,  $Zn^{2+}$ , or  $Zn^{2+}$ . In this case, different cation could have different binding behaviour. Aside from that, solvent also has significantly affected the fluorescence response where  $Zn^{2+}$  in water, TMF, DMSO, ethanol while  $Cd^{2+}$  only in  $CH_3CN$  [60].

Research by [43] also focused on distinguished between  $Zn^{2+}$  and  $Cd^{2+}$  by using Compound 1 that contained amidic acid. Deprotonation of amidic proton of Compound 1 upon binding with  $Zn^{2+}$  resulted in a large bathochromic shift of UV-vis absorption from 300 nm to 344 nm. This indicated greater electron delocalization. Zn-Compound 1 binding gave a strong fluorescent enhancement and shifted from 420nm and 504 nm. The binding involved strong chelation enhanced fluorescence (CHEF), P.E.T. of the amino group of quinoline, and ESIPT from the amidic proton to N atom of quinoline. The coordination geometry of  $Zn^{2+}$  complex was distorted square pyramidal by three chelating nitrogen from one ligand, one oxygen from another ligand, and one more oxygen of  $NO_3^-$  anion.

Given the advantage of fully water-soluble AQZ-2COOH due to the insertion of carboxyl groups, make it a promising receptor for testing  $Zn^{2+}$  in aqueous solution [75]. Crystallography result of binding between  $Zn^{2+}$  and AQZ-2COOH confirmed  $Zn^{2+}$  formed five-coordinated with three N atoms of pyridine, amide, and amine and another two O atoms of carboxyl groups. This five-membered chelation rings made the Zn-complex more stable. The strong and red-shift of UV-Vis absorption explained the deprotonation of amide moiety that lead to reducing the HOMO-LUMO energy gap and the electron transfer reaction of heterocyclic ligand-metal [66].

Fluorescence enhancement of HAQT increased proportionally with the increasing zinc concentration up to 10  $\mu M$  by 5-fold at 488nm, and further addition did not record any further enhancement.  $Zn^{2+}$  was proved coordinated with the HAQT via infrared spectroscopy by noting the disappearance O.H. group at 3419  $cm^{-1}$ , amide carbonyl absorption slightly shifted to 1656  $cm^{-1}$ , and significant difference of N atom of pyridine group at 1300  $cm^{-1}$  and 755  $cm^{-1}$  characteristic hydroxyls [43]. Thus, the plausible reaction between HAQT-Zn involved deprotonation process that increases electron-donating from N atom of 8-amino to quinoline ring and I.C.T. process that transfer of an electron from N atom of the pyridyl group to the metal ion.

Deprotonation and I.C.T. process of L1probe-Zn also similar to the plausible interaction of HAQT-Zn. Fluorescence intensity remarkable shifted from 408 to 489 nm with a quantum yield of 0.138. As in isoemissive point was observed at 427nm. L1 exhibited weak fluorescence while the coordination of L1 as a ligand to metal gave strong fluorescence [53]. Slightly different from Q.P.A. receptor, other than the transferred electron of N atom from quinoline, it also involved the breaking of an intramolecular hydrogen bond, and the chelation ring formed is more firmed and rigid. Therefore, the fluorescence emission spectrum showed new emission at 500 nm with a 106-fold risen [51].

Surprisingly, the crystal structure of PMQA-Zn shown uncommon evidence of binding between 8-aminoquinoline and  $Zn^{2+}$ . Neither N atom of 8-aminoquinoline was bound to zinc even though PMQA formed hexadentate chelate ring with  $Zn^{2+}$ . Those N atoms are critically coordinated to  $Cu^{2+}$  perfectly. PMQA-Cu complexes found to be more stable than PMQA-Zn due to ligands containing nitrogen ligands usually have a higher affinity with zinc, cadmium, and copper. Even though the fluorescence emission quenching when introduced to  $Cu^{2+}$ , this PMQA also provides information for elucidating zinc probes to prevent  $Cu^{2+}$  interferences [62].

### 3.5.2 Detection limit

In analytical chemistry, the detection limit or, in other terms, is the limit of detection (L.O.D.) defined as the lowest concentration of target substance reliably distinguished from the blank [76–78]. As we mentioned earlier, the purpose of this systematic review was to summarize the research design and outcomes of the recognition of zinc ion by 8-amidoquinoline. Herein, the lowest concentration of analyte zinc ion detected was reported. Based on our review, the L.O.D. range of

the included articles was between  $3.36 \times 10^{-8}$  M to  $445 \times 10^{-8}$  M. Therefore, the detection limit of 8-amidoquinoline-based zinc chemosensor was in nanomolar proven these derivatives are highly sensitive to recognized Zn(II) ion.

### 3.5.3 Interferences of other competitive metal cations

There are potential interferences of transition metals, especially metals that belong to the same group (Group 12) or same period (Period 4) as Zn(II) ion in the periodic table. They showed almost similar characteristics to Zn(II),  $3d^{10}$  configuration. Therefore, detection of Zn(II) had suffered from the cross-interference of  $Cd^{2+}$ ,  $Cu^{2+}$ ,  $Co^{2+}$ ,  $Ni^{2+}$ , and  $Hg^{2+}$  [79–81]. Based on [49], when chelation of metal-ligand complex coordinated from a five-membered to a six-membered ring, ligands usually selective for the smaller metal ions compared to the larger metal ions. For example, like T.Q.A. ligands more selective to metal  $Zn^{2+}$  (smaller radii) compared to  $Cd^{2+}$  (larger radii). In this research, they demonstrated selectivity of the ligand to the metal ion radius. They concluded, favourable metal-ligand binding depends on two factors that are the size of metals ion and the size of chelate rings.

Thus, all the included articles did screening and analyzing 8-amidoquinoline derivatives on the study of the interference of the other heavy metals towards zinc detection. Evaluations between those studies on the interference of the transition metals documented in Table 1. None of the studies recorded no interference at all. Overall, trace metals like  $Cd^{2+}$ ,  $Cu^{2+}$ ,  $Co^{2+}$ ,  $Ni^{2+}$ ,  $Hg^{2+}$ ,  $Fe^{2+}$ ,  $Pb^{2+}$  and  $Cr^{3+}$  did interfere in detection of zinc using 8-amidoquinoline derivatives. The only difference in those studies is the interference metals, and the metal ratio to zinc used. Nevertheless, certain studies [20,47,50,58,60,64,65,67] demonstrated that the sensing probe could be used in a real sample due to the metals involved not present or least in biological applications. These exhibited 8-amidoquinoline derivatives are selective to zinc detection due to minor interferences issues.

## 4.0 Conclusions

In this review, we covered tremendous interest in 8-amidoquinoline as  $Zn^{2+}$  probes in chemosensor design. By comparing four criteria in the chosen articles, there is still much scope to improve on the derivative of 8-amidoquinoline as a receptor. Such as fast selection and bio-compatibility, especially in the bio application. Most of the receptors, use nitrogen as the binding site because of its more favourable and yet form relatively simple geometries with  $Zn^{2+}$ . In order to get a better understanding of the diversity of that coordination, complex and geometries need to study further. So, this review could be as a guideline in elucidating, designing, and exploring new 8-amidoquinoline derivatives for future studies to get selective, sensitive, and efficient  $Zn^{2+}$  chemosensors.

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