Check for updates

A Review on Calixarene Fluorescent Chemosensor Agents for Various Analytes

Krisfian Tata Aneka Priyangga, Yehezkiel Steven Kurniawan*, Keisuke Ohto, and Jumina Jumina

Abstract

Calixarenes are well-known supramolecular host molecules with versatile applications. Over the past decades, hundreds of selective and sensitive detections have been reported by employing calixarenes as the chemosensor agent. The detection and quantification of ionic species are crucial as heavy metal ions are harmful to living organisms, while monitoring anions is pivotal in the environmental samples. On the other hand, detecting and quantifying biomolecules and neutral molecules are critical due to their irreplaceable role in human health. In this review, we summarized the application of calixarenes as the supramolecular chemosensor agent for detecting metal ions, anions, biomolecules, and neutral molecules through fluorescent spectroscopy. This review updates the world with the application of calixarene derivatives as fluorescent chemosensors and challenges researchers to design and develop better chemosensor agents in the future.

Keywords: chemosensor; calixarene; fluorescent; supramolecular

1. INTRODUCTION

The design and development of sensitive and selective chemosensor agents have received significant attention from researchers over several years [1]-[5]. A chemosensor agent is a chemical that can provide specific intermolecular interactions with a particular substrate or analyte, producing a detectable signal response. According to the targeted analyte, chemosensor agents can be classified into three classes, i.e., cationic, anionic, and neutral chemosensor agents [6]. Sensing of these analytes by using an optical chemosensor agent had received special attention due to its merits, such as easy sample preparation, quick response rate with high precision, and low-cost analysis [7]. Specifically, optical chemosensors are usually employed by using spectroscopic techniques such as colorimetric and fluorometric methods. Compared to the other spectroscopic techniques, colorimetric and fluorometric methods offer a simple operation with high sensitivity and

can be used as a real-time analysis for a selective detection of analyte [8].

A chemosensor agent is also known as a molecular sensor or probe. Chemosensor agents can be employed in the form of a supramolecular-based compound. In this case, the non-covalent interaction between chemosensor and analyte is usually defined as the host-guest interaction [9]. Chemosensor usually contains at least two parts: the binding site (receptor) and signaling unit (detector). The receptor plays a role as the part for interacting with the analyte to induce signal change. On the other hand, the signaling unit provides a signal response change after the interaction with the analyte. The signaling unit may be composed of the chromophore (in colorimetric sensor) or fluorophore (in fluorometric sensor) [10]. The colorimetric chemosensor agent involves a sensing mechanism that leads to a naked eye color change when interacting with the analyte. Meanwhile, the fluorometric chemosensor agent works through two mechanisms, i.e., fluorescent-OFF à ON and fluorescent-ON à OFF (see Figure 1). The design and development of chemosensor agents with a suitable host-guest interaction to the specific analyte are interesting topics for several decades. Furthermore, the topic of chemosensor also includes the preparation of chemosensor agents through either organic or inorganic synthesis, optical properties, and its analytical application [11].

Chemosensor agent has been widely applied to detect and quantify cations, anions, or neutral molecules in simulated or real sample analysis. As
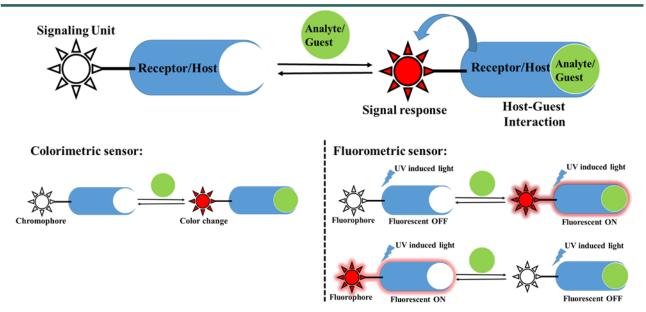
PANDAWA INSTITUTE

Figure 1. The general sensing mechanism of colorimetric and fluorometric chemosensor agents.

an example, detection and quantification of heavy metals are crucial as they are harmful to living organisms. These heavy metals are often found in polluted aquatic samples. Because of that, cation sensing gained significant attention to establish a sustainable future [12]. The detection of anions is also essential due to their important role in biological and environmental ecosystems. The presence of a certain anion in an acceptable amount can be useful in some applications but not in an excessive concentration [13]. Meanwhile, the detection of neutral molecules usually involves recognizing biomolecules such as amino acids and nucleotides [14][15].

Calixarene derivatives are well-known host molecules with versatile applications, including chemosensor agents [16]-[21]. Calixarenes consisted of a macrocyclic oligomer framework resulted from the condensation reaction between formaldehyde and *tert*-butylphenol [22]. Calixarene has a specific ring size that can be controlled by using an ion-template synthesis. The control on the ring size of calixarenes yields calix[4]arene, calix[5]arene, calix[6]arene, and calix[8]arene [23][24]. The conformation of the calixarene can also be controlled in various conformations such as cone, partial cone, 1,2-alternate, and 1,3-alternate [25], as shown in Figure 2. Moreover, the calixarenes can be easily modified on their upper or lower rim [26].

Calixarenes are reported to have good photoluminescence properties; thus, calixarenes have been extensively used as the chemosensor agent. Because of that, a brief review on the application of calixarenes as the fluorescent chemosensor agent is useful to give brief information about the design and development on the chemosensor field. However, the latest review article on the fluorescent chemosensor based on calixarene derivatives was published in 2013 [23]. Furthermore the application of supramolecular calixarenes as fluorescent chemosensor was not discussed in particular in the recent literature. From that report, an updated review specifically on the fluorescent chemosensor based on supramolecular calixarene derivatives has not been available yet as for today. To a certain extent, this review provides a brief update on the utilization of supramolecular-based calixarene derivatives as the fluorometric chemosensor agent for the detection of cations, anions, and neutral molecules. In the present article, we also summarized the performance of each chemosensor agent and provided a brief perspective for future research.

2. COLORIMETRIC AND FLUOROMETRIC DETECTIONS

Colorimetric is the simplest detection method in the chemosensor field. Colorimetric offers the naked eye investigation using a visible spectrophotometer instrument [27]. In the colorimetric method, a chemosensor should contain a chromophore group as the signaling unit. The chromophore is responsible for the color of the

chemosensor in its free form and the specific color change after its interaction with a particular analyte. Therefore, the colorimetric method works by measuring the absorbance change after the addition of the analyte [28]. Because of that, the colorimetric method has a limitation on poor sensitivity and background interference.

In contrast, the fluorometric method is preferable for actual application due to its higher sensitivity than the colorimetric method. The fluorometric method has been widely used to detect and quantify cations, anions, or neutral molecules. The fluorometric technique uses a chemical with a fluorophore unit, in chemosensor application [29]. The fluorometric chemosensor can interact with the analyte through several sensing mechanisms such as intramolecular charge transfer (ICT), photoinduced electron transfer (PET), chelation-induced enhanced fluorescence (CHEF), chelation quenched fluorescence (CHQF), aggregation caused quenching (ACQ), and aggregation-induced emission (AIE) [30]-[35]. Schematic examples for each sensing mechanism are depicted in Figure 3. The different phenomenon leads to a different pathway to detect a certain analyte. However, detection using the fluorometric method generally can be classified into two pathways: Fluorescence OFF and Fluorescence ON. Fluorescence OFF happened when the emission intensity of the free chemosensor agent was quenched due to the addition of a certain analyte. Meanwhile, the Fluorescence ON increases the emission intensity due to the interaction between the chemosensor agent and analyte.

3. CALIXARENE FOR CATION CHEMOSENSOR

The usage of calixarenes for the detection of metal ions have been developed in recent years. For example, Xu and coworkers utilized naphthalimide –calix[4]arene (**1**) for selective detection of Cu^{2+} ions in $MeCN:H_2O$ (9:1 v/v) solvent system. Compound **1** gave the quenching phenomenon at emission wavelength (λ_{em}) of 490 nm (excitation wavelength, λ_{ex} = 435 nm) with the presence of Cu^{2+}. An excellent selectivity was observed over the other metal ions such as Ag^+, Li^+, Na^+, K^+, Rb^+, Cs^+, Ca^{2+}, Cd^{2+}, Co^{2+}, Hg^{2+}, Mg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+}, which was remarkable. The oxygen atoms of calixarene and nitrogen atoms of naphthalimide are responsible for Cu^{2+} binding, generating a 1:1 complex with an association constant (K_a) of 2.9 × 10^4 M^{-1} [36].

Wang and coworkers employed a pyrene-modified calix[4]arene (**2**) for selective detection of Na^+ cation in DMSO:MeCN (1:9 v/v). When the calixarene **2** was excited at 343 nm, its excimer emission signal at 477 nm was quenched, while the monomer emission signal at 375 nm was increased with the presence of Na^+. In contrast, the emission signal was not significantly changed by the addition of the other metal ions such as Li^+, K^+, Cs^+, Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}. This excellent selectivity was caused by the presence of four carbonyls of ester functional group encapsulated the Na^+ ions in an ionophoric cavity. The complexation happened on the calixarene **2** lower rim, thus affecting the pyrene moieties on the upper rim. Calixarene **2** acted as a molecular tweezer with an on-off mechanism controlled with Na^+ ions. Initially, the pyrene moieties overlapped through π-π stacking, thus
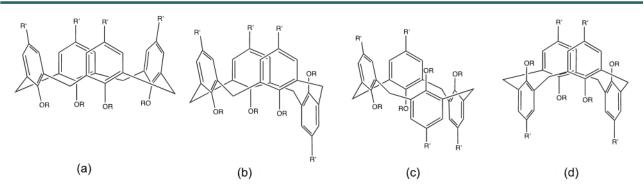

Figure 2. The conformational isomers of calixarenes; a) cone, b) partial cone, c) 1,2-alternate, d) 1,3-alternate.
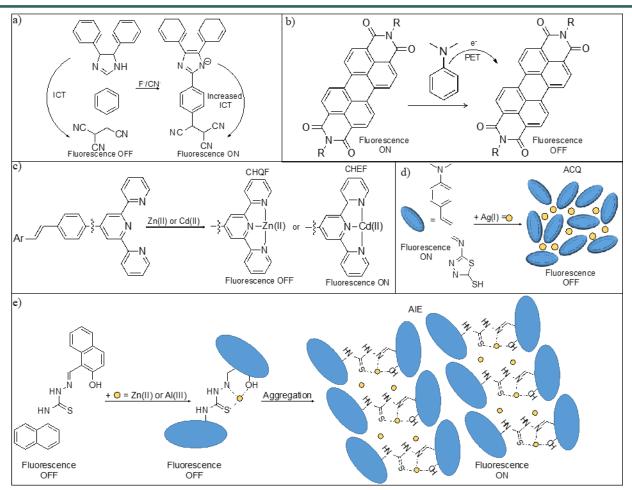
Figure 3. Schematic fluorescence sensing mechanisms, i.e., a) ICT, b) PET, c) CHEF and CHQF, d) ACQ, and e) AIE.

generating an excimer emission signal at 477 nm. In contrast, complexation with Na$^+$ ions at the lower rim of calixarene **2** forced the pyrenes to stay away from each other; thus, the excimer emission signal was quenched, but the monomer emission signal was activated. The calixarene **2** formed a 1:1 complex with Na$^+$ ions giving a K_a value of 2.2 × 10^3 M^{-1} [37].

Dinda and coworkers used the nitrobenzoxadiazole appended calix[4]arene derivative (**3**) for selective recognition of trivalent metal ions, i.e., Cr^{3+}, Fe^{3+}, and Al^{3+}. The detection of these trivalent metal ions occurred through a fluorescence ON as the fluorescence quantum yield of calixarene **3** was significantly enhanced after the addition of metal ions. The calixarene **3** had a low emission intensity at 550 nm (λ_{ex} = 470 nm); however, the addition of M^{3+} increased its fluorescence intensity in a 4-fold increment of quantum yield. This phenomenon happened because of chelation enhanced fluorescence intensity between calixarene **3** and metal ions. From the

spectroscopic study, the M^{3+} ions interacted with benzofurazan rings, amide oxygens, and phenoxy oxygen atoms of calixarene **3**. The K_a value of this chelation was 1.0 × 10^4 M^{-1} suggesting a moderate strength complexation. The sensitivity of calixarene **3** was shown from a low limit detection (LoD) value (5 µM). The formed complex between calixarene **3** and M^{3+} ions was reversible by the addition of H$_2$PO$_4^-$. Therefore, this chemosensor agent can be reused for the detection and quantification of these trivalent metal ions. Furthermore, a real application of calixarene **3** for the detection of M^{3+} ions was also established within MCF-7 cells [38].

Zhan and coworkers used the anthraquinone-calix[4]arene (**4**) for selective detection of Ca^{2+} ions. The selective detection of Ca^{2+} ions was found over the other metal ions such as Ag$^+$, Na$^+$, K$^+$, Li$^+$, Cs$^+$, Mg^{2+}, Sr^{2+}, Ba^{2+}, Cu^{2+}, Cd^{2+}, Ni^{2+}, Mn^{2+}, Co^{2+}, and Zn^{2+}. The sensing method was performed in acetonitrile media, and it was found that the interaction between calixarene **4** and Ca^{2+} ions

increased the emission intensity at 510 nm (λ_{ex} = 390 nm). The addition of Ca^{2+} ions at various concentrations gradually increased its fluorescence intensity yielding a LoD value of 50 µM. The fluorescence ON phenomenon was generated from a 1:1 complexation reaction between calixarene **4** and Ca^{2+} with a K_a value of 1.2×10^4 M^{-1}. The Ca^{2+} ions bind to the nitrogen atoms of triazole in calixarene **4**, leading to a restriction of the PET and an increase in emission intensity [39].

Li and coworkers employed calixarene **5** for the detection of Fe^{3+} and Cu^{2+} ions in H_2O:MeOH (1:1 v/v) media. The fluorescence intensity of calixarene **5** was significantly quenched by the addition of Fe^{3+} and Cu^{2+} ions. Meanwhile, the addition of other metal ions such as Co^{2+}, Ni^{2+}, Zn^{2+}, Mn^{2+}, Mg^{2+}, and Ba^{2+} did not significantly change the fluorescence intensity of calixarene **5**. The calixarene **5** formed a 1:1 complex structure with either Fe^{3+} or Cu^{2+} ions only at a low concentration
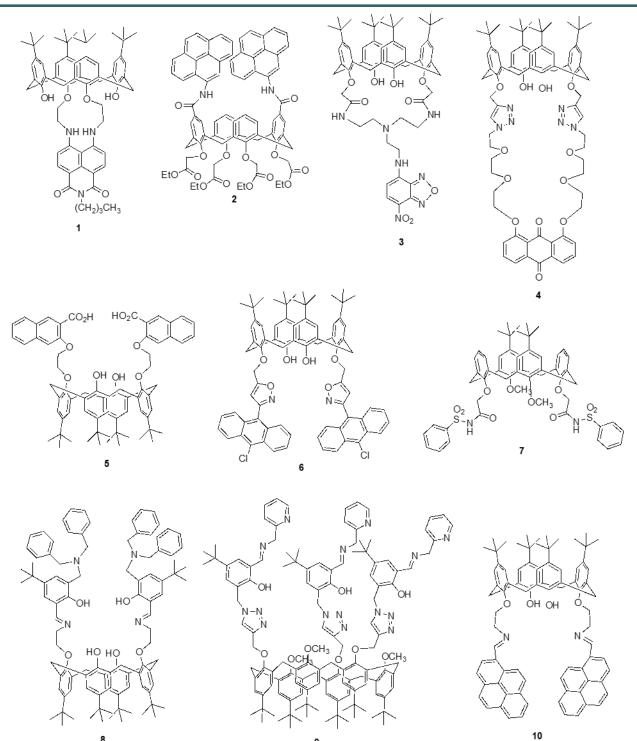

Figure 4. Chemical structures of calixarene-based chemosensor agents **1**–**10** for cations sensing.

Table 1. Performance of calixarene-based chemosensor agents for cation sensing.

Calixarene	Sensing media	LoD (nM)	K_a (M^{-1})	Analyte	Reference
1	MeCN:H$_2$O (9:1 v/v)	n/a	2.9×10^4	Cu^{2+}	[36]
2	DMSO:MeCN (1:9 v/v)	n/a	2.2×10^3	Na$^+$	[37]
3	n/a	5,000	1.0×10^4	Cr^{3+}, Fe^{3+}, and Al^{3+}	[38]
4	MeCN	50,000	1.2×10^4	Ca^{2+}	[39]
5	H$_2$O:MeOH (1:1 v/v)	n/a	n/a	Fe^{3+} and Cu^{2+}	[40]
6	MeCN:CHCl$_3$ (1000:4 v/v)	n/a	1.6×10^4	Cu^{2+}	[41]
7	H$_2$O:MeCN (1:1 v/v)	n/a	n/a	Hg^{2+}	[42]
8	MeOH	0.69	n/a	Zn^{2+}	[43]
9	n/a	490	3.7×10^4	La^{3+}	[44]
10	DCM:MeCN (1:1 v/v)	490	n/a	Pb^{2+}	[45]

*n/a: not available

(less than 1 µM). At a higher concentration of the metal ions lead to the formation of a different complex stoichiometry. This phenomenon in fluorescence quenching was also highly related to the pH value of the aqueous media [40].

Chang and coworkers used the modified calix[4]arene with anthracene-isoxazolymethyl group (6) at the lower rim for the detection of Cu^{2+} ions. The calixarene 6 showed two emission peaks at 511 nm (excimer) and 430 nm (monomer) with the λex of 375 nm. The calixarene 6 showed selectivity and sensitivity in the detection of Cu^{2+} in CH$_3$CN:CHCl$_3$ (1000:4, v/v) solvent system, through coordination with isoxazole moieties. The selectivity was compared to the 14 metal ions including Ag$^+$, Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Ba^{2+}, Pb^{2+}, Hg^{2+}, Cd^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+}, and Cr^{3+}. The fluorescence emission intensity was quenched only with the addition of Cu^{2+} ions, while the other cations did not significantly change the fluorescence spectra of the free ligand. The calixarene 6 formed complex with Cu^{2+} with a 1:1 ratio with a K_a value of 1.6×10^4 M^{-1} [41].

Arena and coworkers utilized calix[4]arene bearing N-(phenyl)sulfonylcarboxamide (7) for selective detection of Hg^{2+} ions in H$_2$O:MeCN (1:1 v/v) media. The presence of Hg^{2+} ions quenched the fluorescence intensity of calixarene 7. The sensing mechanism occurred through the Turn-OFF fluorescence at λem of 312 nm (λex = 273 nm). The calixarene 7 showed high selectivity for Hg^{2+} ions

over the other heavy metal ions such as Pb^{2+} and Cd^{2+}. Unfortunately, the sensitivity for Hg^{2+} detection has not been evaluated yet [42].

Joseph and coworkers investigated the application of calix[4]arene 8 to detect Zn^{2+} ions. The calixarene 8 showed an excellent sensitivity for Zn^{2+} ions with the LoD value of 0.69 nM in methanol media, which was remarkable. The emission intensity of calixarene 8 at 380–620 nm (λex = 370 nm) was significantly increased by the presence of Zn^{2+} ions. Additionally, calixarene 8 also exhibited good selectivity for the detection of Zn^{2+} ions. The addition of the other metal ions such as Na$^+$, K$^+$, Mn^{2+}, Co^{2+}, Ca^{2+}, Mg^{2+}, and Cd^{2+} did not significantly change the emission intensity of calixarene 8. The addition of these metal ions gave a negligible interference for Zn^{2+} detection, indicating a good selectivity. The Fluorescence turn-ON phenomenon happened due to the binding of Zn^{2+} to the imine and phenolic moieties of calixarene 8 blocking the PET to the salicylyl moiety [43].
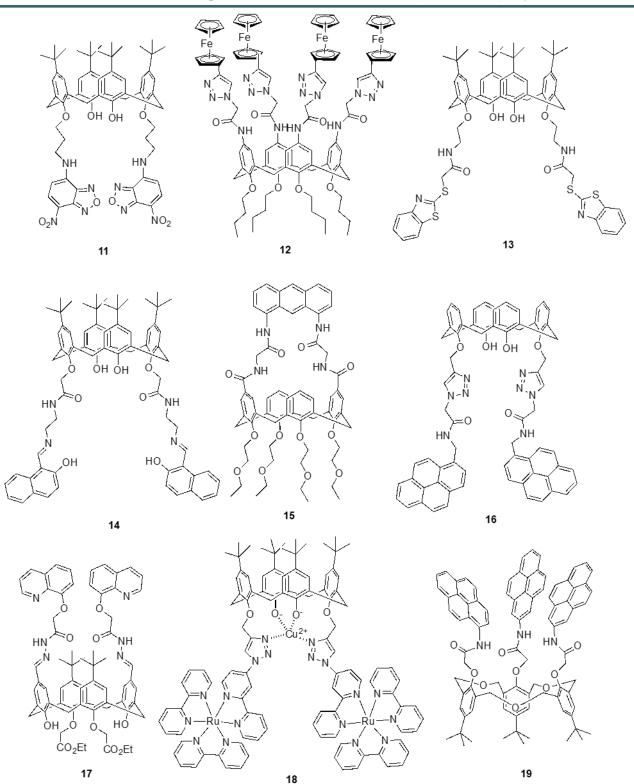
Mummidivarapu and coworkers employed a calix[6]arene with triazole linked picolimine conjugate (9) for the detection of La^{3+} ions. Calixarene 9 showed a selective and sensitive detection for La^{3+} ions with a LoD value of 490 nM. The sensing mechanism happened through fluorescence turn-ON on the emission intensity of 450 nm (λex = 330 nm). The addition of the other trivalent metal ions such as Pr^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+},
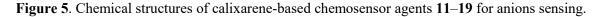
Gd^{3+}, Dy^{3+}, and Ho^{3+} did not significantly increase the emission intensity. Calixarene **9** complexed with La^{3+} ions with a K_a value of 3.7×10^4 M^{-1}. In this case, the imino-phenolic and the pyridyl moieties play an important role in binding with La^{3+} ions. Complex formation between calixarene **9** and La^{3+} ions triggered the inhibition of imine isomerization and excited-state proton transfer

(ESPT), leading to an increase in the fluorescence emission [44].

Kumar and coworkers applied the pyrene-appended calix[4]arenes derivative (**10**) for the fluorometric detection of Pb^{2+} ions in DCM:MeCN (1:1 v/v) media. Calixarene **10** exhibited excellent sensitivity and selectivity for detecting Pb^{2+} ions at λ_{em} of 498 nm (λ_{ex} = 350 nm). By addition of Pb^{2+}

Figure 5. Chemical structures of calixarene-based chemosensor agents **11**–**19** for anions sensing.

Table 2. Performance of calixarene-based chemosensor agents for anion sensing.

Calixarene	Sensing media	LoD (nM)	K_a (M^{-1})	Analyte	References
11	THF	100	1.6×10^3	F$^-$	[46]
12	MeCN:CH$_2$Cl$_2$ (1:1 v/v)	2,980	5.35×10^8	F$^-$	[47]
13	MeOH	5,000	1.49×10^{-4}	I$^-$	[48]
14	n/a	4,500	15.6×10^2	I$^-$	[49]
15	MeCN:CHCl$_3$ (99.6:0.4 v/v)	n/a	n/a	F$^-$	[50]
16	n/a	n.a	n/a	H$_2$PO$_4^-$, F$^-$, and AcO$^-$	[51]
17	MeCN:H$_2$O (7:3 v/v)	1,260	n/a	CN$^-$	[52]
18	MeCN:H$_2$O (8:2 v/v)	350	n/a	S^{2-}	[53]
19	THF:H$_2$O (7:3 v/v)	164	n/a	I$^-$	[54]

*n/a: not available

ions, the excimer emission intensity of calixarene **10** at 498 nm was gradually quenched, with a gradual increment of emission signal at 415 nm. This hypsochromic shifting was attributed to the deprotonation of phenolic groups of calixarene **10**. The addition of other metal ions such as Ag$^+$, Li$^+$, Na$^+$, K$^+$, Zn^{2+}, and Hg^{2+} (in perchlorate salts) gave no significant fluorescence change for calixarene **10**. Calixarene **10** gave a LoD value for detecting Pb^{2+} as low as 490 nM as calculated from the ratiometric plot of I$_{415}$/I$_{498}$. Calixarene **10** formed a 1:1 complex with Pb^{2+} ions through the imino group, causing an ICT from pyrene to the imino groups [45].

4. CALIXARENE FOR ANION CHEMOSENSOR

Uttam and coworkers employed a calix[4]arene conjugated with 1,3-dibenzooxadiazole (**11**) for the detection of fluoride anion (F$^-$) in tetrahydrofuran (THF) solvent. Calixarene **11** could selectively detect F$^-$ anion over 15 other anions such as bromide (Br$^-$), chloride (Cl$^-$), iodide (I$^-$), azide (N$_3^-$), thiocyanate (SCN$^-$), bicarbonate (HCO$_3^-$), dihydrogen phosphate (H$_2$PO$_4^-$), carbonate (CO$_3^{2-}$), nitrite (NO$_2^-$), nitrate (NO$_3^-$), sulfate (SO$_4^{2-}$), pyrophosphate (P$_2$O$_7^{4-}$), perchlorate (ClO$_4^-$), and bisulfate (HSO$_4^-$). Calixarene **11** also exhibited a sensitive detection of F$^-$ with a LoD value of 100 nM. In the detection of F$^-$ ions using calixarene **11**, a 1:1 complex structure was formed with a K_a value of 1.6×10^3 M^{-1}; thus, the λ_{em} at 520 nm (λ_{ex} = 460 nm) was significantly quenched. From the experimental-NMR and computational-density functional theory (DFT) studies, it was found that the F$^-$ ion was coordinated through extended hydrogen bonds with dibenzooxadiazole and phenoxy oxygen atoms of calixarene **11**. These chelations became the reason for such excellent selectivity of F$^-$ ions complexation and sensing. The chemosensor **11** offered good reusability as it can be decomplexed by the addition of Ca^{2+} ions with still good sensing capability even at 10 cycle sensing. Furthermore, a biological application for detecting F$^-$ ions in the HeLa cells was also performed. The results demonstrated that calixarene **11** exhibited great application in the THF media as well as in HeLa cells [46].

Hosseinzadeh and coworkers used the ferrocene-triazole-amide functionalized calix[4]arene (**12**) for the detection of F$^-$ in MeCN:DCM (1:1 v/v) media. Calixarene **12** showed a selective and sensitive detection of F$^-$ anion compared to the other anion including acetate (AcO$^-$), Cl$^-$, Br$^-$, ClO$_4^-$, NO$_3^-$, H$_2$PO$_4^-$, and HSO$_4^-$. The selectivity of calixarene **12** was shown from the enhancement in fluorescence emission intensity at 418 nm (λ_{ex} = 290 nm). In addition, the LoD value for F$^-$ detection was 2.98 μM. The extended hydrogen bonds between F$^-$ ions and amide and triazole protons of calixarene **12** corresponded to the

binding site in the sensing mechanism, as revealed by the NMR titration study. The calixarene 12 and F^- ions formed a 1:2 complex structure with a K_a value of 5.4×10^8. The complexation was formed through the hydrogen bond between F^- from both amide and triazole protons in calixarene **12** [47].

Gómez-Machuca and coworkers synthesized a calix[4]arenes with azolyl moieties (**13**) for the detection of I^- anion in MeOH. Calixarene **13** gave both sensitive and selective detection of I^- compared to the other anions (F^-, HSO_4^-, N_3^-, NO_2^-, NO_3^-, SCN^-, ClO_4^-, Br^-, CN^-, Cl^-, $CH_3CO_2^-$, $CF_3SO_3^-$). The tetrabutylammonium salts were used to avoid any cationic complexation with calixarene **13**. In addition, calixarene **13** gave a quenching response at λ_{em} of 330 nm (λ_{ex} = 225 nm) by the addition of I^- anion yielding a LoD value of 5 μM. Calixarene **13** formed a 1:1 complex with I^- ion through hydrogen bonds with a K_a value of 1.5×10^{-4} M^{-1}. From the NMR titration study, the signal of N-H amide and Ar-H of benzoxazole moieties changed clearly. The N-H signal was shifted to a higher chemical shift due to an extended hydrogen bond with I^- ions. Meanwhile, the changed Ar-H benzoxazole signals occurred due to the fixed and rigid structure of benzoxazole substituents after I^- complexation reaction [48].

Memon and coworkers utilized a calix[4]arene bearing naphtyhylimino moiety (**14**) for sensitive and selective detection of Au^{3+} cation and I^- anion.

The fluorescence response in the detection of both ions occurred through a quenching phenomenon at its emission intensity at λ_{em} 360 nm (λ_{ex} = 330 nm). The LoD value for the detection of Au^{3+} and I^- were 15 and 4.5 μM respectively. The quenching response was due to a 1:1 complexation reaction between calixarene **14** and either Au^{3+} or I^- which gave a K_a value of 8×10^2 or 16×10^2 M^{-1}, respectively. The imine (C=N), amide carbonyl (C=O), and hydroxyl functional groups were important in the Au^{3+} sensing. Meanwhile, the hydroxyl and amide nitrogen atoms of calixarene **14** interacted with I^- anion through the extended hydrogen bonds [49].

Miao and coworkers applied a calix[4]arene with diaminoanthracene group (**15**) for the detection of AcO^- in MeCN:CHCl$_3$ (99.6:0.4 v/v). The tetrabutylammonium salts were used to avoid any cationic complexation with calixarene **15**. Calixarene **15** can selectively detect AcO^- over the other anions such as Cl^-, Br^-, I^-, NO_3^-, HSO_4^-, and $H_2PO_4^-$. The addition of AcO^- to calixarene **15** yielded a quenching of emission signal at λ_{em} 438 nm (λ_{ex} = 370 nm). The quenching happened through a free PET process between calixarene **15** and AcO^- anion. Meanwhile, no spectral changes were observed by the addition of other anions. Furthermore, the detection of AcO^- occurred through hydrogen bonds between -NH and 9-H of anthracene as confirmed from the ^{1}H-NMR titration
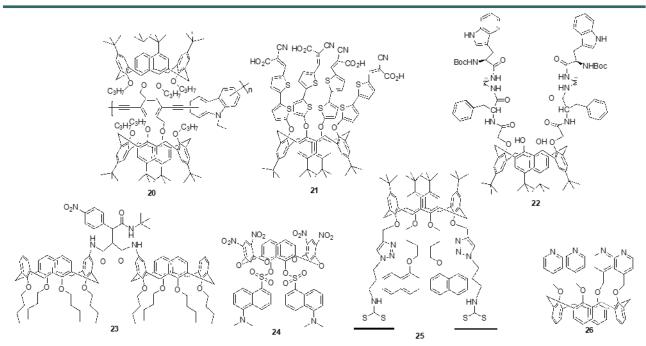

Figure 6. Chemical structures of calixarene-based chemosensor agents on **20–26** for neutral molecules sensing.

Table 2. Performance of calixarene-based chemosensor agents for anion sensing.

Calixarene	Sensing media	LoD (µM)	K_a (M^{-1})	Detection	References
20	CHCl$_3$	3.49–107	n/a	Nitroaromatics	[56]
21	H$_2$O	n/a	$3.5 \times 10^3 - 1.4 \times 10^5$	Amino acids	[57]
22	MeCN	n/a	$9.1–56.5 \times 10^1$	Amino alcohols	[58]
23	H$_2$O	24.5×10^{-3}	3.7×10^5	NADH	[59]
24	n/a	3.81×10^{-3}	1.3×10^5	PM	[60]
25	MeCN	0.10	1.2×10^5	MC	[61]
26	MeOH:iPrOH (1:1 v/v)	2.25	n/a	glyphosate	[62]

*n/a: not available

study [50].

Hung and coworkers prepared a calix[4]arene owing to pyrenylacetamide functional group (16) for the detection of H$_2$PO$_4^-$, F$^-$, and AcO$^-$ anions. Three different binding modes were observed for these anions. Static excimer with large and small charge transfer occurred for F$^-$ and AcO$^-$ anions, respectively. Meanwhile, an increment in monomer emission of calixarene 16 happened for H$_2$PO$_4^-$ sensing. The dynamic excimer emission of calixarene 16 (λ_{em} = 482 nm) was quenched by the addition of F$^-$ at a low concentration. However, in an excess concentration of F$^-$, the emission signal at 472 nm was increased significantly. This phenomenon was caused by the formation of a strong extended hydrogen bond between F$^-$ and calixarene 16 through its amide group, leading to a generation of pyrene dimers. On the other hand, H$_2$PO$_4^-$ sensing showed an opposite mechanism as the monomer emission at 472 nm was enhanced, but the excimer emission at 482 nm was decreased [51].

Chawla and coworkers investigated the application of calix[4]arene bearing quinoline moiety (17) for the detection of Cu^{2+} and CN$^-$ ions in MeCN:H$_2$O (7:3 v/v) media. Calixarene 17 could selectively detect Cu^{2+} over the other metal ions such as Zn^{2+}, Pb^{2+}, Co^{2+}, Ni^{2+}, Na$^+$, Li$^+$, Fe^{3+}, Hg^{2+}, Cd^{2+}, K$^+$, Mn^{2+}, and Ag$^+$. The addition of Cu^{2+} leads to a significant quenching at λ_{em} of 405 nm (λ_{ex} = 315 nm) of calixarene 17. The sensitivity of calixarene 17 for Cu^{2+} detection was shown by its

LoD value as low as 0.4 µM. Interestingly, the addition of Cu^{2+} followed by CN$^-$ ion leads to a gradual increment of emission signal at 405 nm. It means that the calixarene 17 could also be used for the detection of CN$^-$ through the formation of Cu^{2+}-calixarene 17 complex. The LoD value for CN$^-$ detection was 1.26 µM. Furthermore, a selective detection for CN$^-$ was achieved over F$^-$, Cl$^-$, Br$^-$, I$^-$, S^{2-}, AcO$^-$, CO$_3^{2-}$, HSO$_4^-$, and H$_2$PO$_4^-$. The CN$^-$ detection was stable in a pH region of 6–8. Lower pH value protonated quinoline nitrogen atoms while higher pH value formed a hydroxide complex of $[Cu(OH)_m]^{(2-m)+}$. The selectivity of Cu^{2+}-calixarene 17 complex for CN$^-$ detection happened as the Cu^{2+} ion itself was able to form a very stable metal complex with CN$^-$ anion. Additionally, the chelation of calixarene 17 aided in locking the CN$^-$ anion through extended hydrogen bonds with quinoline and amide nitrogen atoms, thus providing an excellent sensing site for CN$^-$ anion [52]. These results are useful for developing a dual-response chemosensor agent for the detection of cation and anion with high selectivity and sensitivity.

Ramachandran and coworkers designed calix[4]arene 18 for the detection of Cu^{2+} and S^{2-} ion in MeCN:H$_2$O (8:2 v/v) media. Free calixarene 18 showed a photoluminescence property at λ_{em} of 637 nm (λ_{ex} = 457 nm). The addition of Cu^{2+} led to a gradual quenching by increasing Cu^{2+} concentration. The LoD value of Cu^{2+} was 4.11 µM, with a K_a value of 2.3×10^4 M^{-1}. Calixarene 18 showed a high selectivity for Cu^{2+} detection

compared to the other cations such as Na^+, Ag^+, Fe^{2+}, Hg^{2+}, Mg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, Ca^{2+}, Co^{2+}, Fe^{3+}, and Al^{3+}. For anion sensing, the Cu^{2+}-calixarene 18 complex showed a selective detection of S^{2-} anion over the other anions (AcO^-, CN^-, CO_3^{2-}, F^-, HPO_4^-, HSO_4^-, NO_2^-, NO_3^-, HO^-, and SO_3^{2-}), which was remarkable. The detection limit of S^{2-} was estimated to be 0.35 μM [53].

Xie and coworkers employed the hexahomotrioxacalix[3]arene (19) for the detection of I^- in a $THF:H_2O$ mixture (7:3 v/v). Calixarene 19 was found to be a selective and sensitive chemosensor agent for the detection of I^- ion. Calixarene 19 showed a high emission intensity at 484 nm (λ_{ex} = 346 nm). The presence of I^- ion leads to a significant quenching at this emission intensity compared to the other anions such as F^-, Cl^-, Br^-, AcO^-, SO_3^{2-}, SO_4^{2-}, HSO_3^-, NO_3^-, and CO_3^{2-}. The binding mechanism for I^- sensing occurred due to the hydrogen amide group of calixarene 19 to form the extended hydrogen bonds with a K_a value of 2.5 $\times 10^2$ M^{-1}. The fluorescence titration study showed that the addition of I^- at higher concentration leads to a gradual decrease in emission signal at 484 nm yielding a LoD value of 164 nM. The sensitivity of I^- was better than using atomic absorption spectroscopy or chromatography, which was remarkable. Furthermore, the I^- sensing was satisfying over a broad range pH value of 2-11 [54].

5. CALIXARENE FOR NEUTRAL MOLECULE CHEMOSENSOR

Detection of neutral analyte is also pivotal as carnitine, nucleoside triphosphate, dopamine, tryptophan, and other biomolecules are essential in the metabolism system, and genetic expression [55]. On the other side, organic molecules such as nitroaromatic and polyaromatic hydrocarbons are also critical to be monitored due to their carcinogenic and explosive properties. Barata and coworkers used the calix[4]arene-modified carbazole polymer (20) for the sensor of the nitroaromatic explosive compounds in $CHCl_3$ media. Calixarene 20 showed high sensitivity towards nitroaromatic compounds such as picric acid (PA), 2,4,6-trinitrotoluene (TNT), 2,4-dinitrotoluene (DNT), and nitrobenzene (NB). The emission signal of calixarene 20 at 430 nm (λ_{ex} =

360 nm) was gradually quenched by the addition of these nitroaromatic compounds at a higher concentration. Calixarene 20 exhibited the highest sensitivity for TNT detection. The sensitivity of calixarene 20 was shown from the LoD value of 3.49, 26.4, 52.7, 107 μM for PA, TNT, DNT, and NB, respectively. The PET mechanism caused the quenching phenomenon as the ligand has a conjugated electron system (electron-rich) and nitroaromatic as an electron-deficient compound [56].

Xu and coworkers employed a calix[4]arene modified bithiophene (21) for the detection of amino acids in water. Calixarene 21 gave a response for acidic amino acids, i.e., aspartic acid (Asp) and glutamic acid (Glu), through a fluorescence quenching phenomenon at λ_{em} of 566 nm (λ_{ex} = 400 nm). On the other hand, calixarene 21 gave a response for basic amino acids, i.e., lysine (Lys) and arginine (Arg), through a fluorescence ON at the same λ_{em}. These responses were selective over the other amino acids. Although a quantitative detection of amino acids using calixarene 21 has not been further studied, calixarene 21 showed a moderately strong complexation with K_a value of 7.9 $\times 10^4$ M^{-1}, 1.4 $\times 10^5$ M^{-1}, 3.5 $\times 10^3$ M^{-1}, and 8.1 $\times 10^3$ M^{-1} for Asp, Glu, Lys, and Arg, respectively [57].

Qing and coworkers investigated a calix[4]arenes bearing L-tryptophan unit (22) for the detection of amino alcohol compounds in MeCN. Calixarene 22 showed a weak emission signal at 456 nm (λ_{ex} = 368 nm). The addition of phenylglycinol and phenylalaninol to the calixarene 22 significantly increased the emission signal due to π-π stacking interactions. The K_a value of the complex between calixarene 22 with phenylglycinol and phenylalaninol was found to be 5.6 $\times 10^2$ M^{-1} and 9.1 $\times 10^1$ M^{-1}, respectively. However, the quantitative detection of these amino alcohol compounds has not been studied yet [58].

Zadmard and coworkers utilized a dimer of calix[4]arene (23) for the detection of NADH in an aqueous solution. NADH is an important biomolecule used in the metabolism system consisted of adenine, nicotinamide, and ribosome residues connected to a phosphate group. Calixarene 23 exhibited excellent selectivity for the detection of NADH over other biomolecules (AMP,

ADP, ATP, NAD, NADP, NADPH, uracil, cytosine, adenine, and guanine), which was remarkable. The emission signal at 325 nm (λ_{ex} = 275 nm) was significantly quenched by the addition of NADH only, yielding an LoD value of 24.5 nM. Calixarene **23** could form a 1:1 complex with a high K_a value of 3.7×10^5 M^{-1} [59].

Panchal and coworkers employed a bidansylatedoxacalix[4]arene (**24**) for pendimethalin (PM) detection. This analyte is mainly found in herbicides and considered to be a toxic compound for soil and aquatic microorganisms. The emission signal of calixarene **24** at 466 nm (λ_{ex} = 251 nm) was quenched by the addition of PM. In contrast, the addition of other pesticides such as propanil, sulfosulforon, pretilachlor, ametryn, tertbutryn, tebuconazole, clodinofop propargyl, atrazine, metalaxyl, simetryn, simazine, thiophenate methyl, and tricyclazole did not show a significant change in fluorescent emission. This result indicated an excellent selectivity of calixarene **24** for PM detection with a LoD value of 3.81 nM. Calixarene **24** could form a 1:1 complex with PM giving a K_a value of 1.3×10^5 M^{-1} [60].

Zeng and coworkers used a naphthol appended calix[4]arene (**25**) for the detection of metolcarb (MC) in MeCN media. Calixarene **25** showed high selectivity for the detection of MC over various analytes such as carbosulfan, pirimicarb, carbaryl, carbofuran, and isoprocarb. The addition of MC leads to a significant increment of the emission signal at 340 nm (λ_{ex} = 265 nm) with the LoD value of 0.1 µM. The 1:1 complex structure was generated between calixarene **25** and MC during the sensing process with a K_a value of 1.2×10^5 M^{-1} [61].

Yu and coworkers used the tetrapyridylcalix[4] arene (**26**) modified metal-organic framework for the detection of glyphosate in MeOH:*i*PrOH (1:1 v/ v) solvent system. The glyphosate was used for the representative organophosphate pesticide which often used in the agricultural field. The accumulation of glyphosate in water and crops is harmful due to its toxic effect. Therefore, the detection of this compound is critical to be established. Calixarene **26** yielded a high selectivity toward glyphosate compared to the other interfering analytes such as phenylphosphonic acid,

(aminomethyl)phosphonic acid, formic acid, acetic acid, benzoic acid, oxalic acid, and phosphate ions. In addition, the presence of inorganic ions such as K$^+$, Na$^+$, Zn^{2+}, Ba^{2+}, Sr^{2+}, Mg^{2+}, Co^{2+}, Ca^{2+}, Cl$^-$, Br$^-$, I$^-$, SO$_4^{2-}$, and NO$_3^-$ did not interfere the glyphosphate sensing using calixarene **26**, which was remarkable. The emission signal at 329 nm (λ_{ex} = 281 nm) was significantly enhanced by the addition of glyphosate to give an LoD value of 2.25 µM [62].

6. PERSPECTIVE

So far, the development of supramolecular calixarenes as the fluorescent chemosensor agent exhibits a high selectivity and sensitivity for a certain analyte. Calixarene serves as an ideal framework for either ion or molecule discrimination. Furthermore, a proper modification on either at the upper or lower rim can provide a desired binding site for the particular analyte. The modification depends on the targeted analyte to be detected, which may be cation, anion, or neutral molecule. The different nature of these analytes will influence their interaction with the chemosensor agent.

In general, the mechanism for cation detection usually involves the complexation through electrostatic and/or ion-dipole interactions. However, the different types of cation required different binding sites in the chemosensor agent indeed. For example, the detection of Cu^{2+} is preferable by using the –NH (amino) and oxygen atoms as -OH phenolic and ether moieties. These moieties provide a good binding site for Cu^{2+} ions. The detection of Na$^+$ is preferable by using a functional group containing oxygen from ether, ester, and carbonyl moieties. To detect trivalent cations (Cr^{3+}, Fe^{3+}, and Al^{3+}), the presence of –OH phenolic, ether, ester, and carbonyl groups shall be considered. For Ca^{2+} and La^{3+}, a good detection could be achieved by using a specific triazole group. For Hg^{2+} heavy metal detection, it is advisable that sulfonamide-based calixarene is employed as the receptor. The presence of imine groups at calixarene was found to be important for Zn^{2+} and Pb^{2+} ions detection.

On the other side, the sensing mechanism of anion mainly happened through either extended

hydrogen bond or ion-dipole interactions. Since the anion is an electron-rich species, the binding site used in the sensing for certain anions should be positive or partially positive in charge. Therefore, the easily protonated functional groups shall be used as the binding site for the anion. For example, the detection of F^- required the presence of -OH phenolic, amine, and amide. Besides these functional groups, the presence of the C=N (imine) group is important for the detection of I^-. For the detection of AcO^- and $H_2PO_4^-$, the presence of amide and OH phenolic groups is important. Another mechanism for anion sensing is through the displacement mechanism involving the formation of ligand-metal complex, which then decomplexed by the presence of anion as the analyte. In this case, the anion should form a stronger interaction with the cation. For example, CN^- and S^{2-} strongly interact with Cu^{2+} ions demonstrating that a Cu^{2+}-ligand complex is promising for detecting these anions.

In the detection of the neutral molecules, the mechanism usually involving the hydrogen bond, π-π stacking, and electrostatic interactions. For example, the detection of nitroaromatic compounds can be achieved by using carbazole moiety as it provides the electrostatic, CH-π, and π-π interactions with nitroaromatic compounds. Cyano-acrylic acid moiety could provide a good hydrogen bond interaction with amino acid compounds. Amide group is good for providing a suitable electrostatic interaction for a heterocyclic biomolecule such as NADH. For the application in agricultural scope, the dansyl chloride, naphthol, and pyridyl moieties could provide a strong π-π stacking interaction with these analytes.

7. CONCLUSIONS

The design and development of sensitive and selective chemosensor agents have received significant attention from researchers over the past several years. Chemosensor agent has been widely applied to detect and quantify cation, anion, or neutral molecules in simulated or real sample analysis. Employing an optical chemosensor agent through fluorescence spectroscopy has received special attention due to its merits: easy sample preparation, quick response rate with high precision, and low-cost analysis. Calixarenes have good photoluminescence properties with excellent selectivity and sensitivity, thus calixarenes have been extensively used as the chemosensor agent. A proper modification on either at the upper or lower rim can provide a desired binding site for the particular analyte. In general, the mechanism for cation detection usually involving the complexation through electrostatic and/or covalent interactions. On the other hand, the sensing mechanism of anion mainly happened through either hydrogen bonds or dipole-dipole interactions between the anion as an electron-rich species with the positively charged binding site of calixarenes. Meanwhile, the sensing mechanism of biomolecules and neutral analytes usually involving the hydrogen bond, π-π stacking, and electrostatic interactions. These results may provide a useful insight into the design and development of chemosensor agents based on calixarene derivatives.

AUTHOR INFORMATION

Corresponding Author

Yehezkiel Steven Kurniawan — Ma Chung Research Center for Photosynthetic Pigments, Universitas Ma Chung, Malang-65151 (Indonesia); Department of Chemistry, Universitas Gadjah Mada, Yogyakarta-55281 (Indonesia);
orcid.org/0000-0002-4547-239X
Email: yehezkiel.steven@machung.ac.id

Authors

Krisfian Tata Aneka Priyangga — Ma Chung Research Center for Photosynthetic Pigments, Universitas Ma Chung, Malang-65151 (Indonesia);
orcid.org/0000-0002-4119-2470
Keisuke Ohto — Department of Chemistry and Applied Chemistry Saga University, Saga-8408502 (Japan);
orcid.org/0000-0002-5284-5019
Jumina Jumina — Department of Chemistry, Universitas Gadjah Mada, Yogyakarta-55281 (Indonesia);
orcid.org/0000-0003-2604-7838

ACKNOWLEDGEMENT

REFERENCES

[1] M. R. G. Fahmi, Y. S. Kurniawan, L. Yuliati, and H. O. Lintang. (2019). "Selective Optical Chemosensors of Fe^{3+} Ions using 1H-Indole-2,3-dione". *AIP Conference Proceeding*. **2175** : 020062. 10.1063/1.5134626.

[2] A. A. Nugroho, Y. S. Kurniawan, and L. Yuliati. (2020). "Acetylacetone as A Potential Chemosensor for Rapid Detection of Cu(II) Ions In Aqueous Media". *IOP Conference Series: Materials Science and Engineering*. **833** : 012027. 10.1088/1757-899X/833/1/012027.

[3] D. Ariyanti, D. Iswantini, P. Sugita, N. Nurhidayat, H. Effendi, A. A. Ghozali, and Y. S. Kurniawan. (2020). "Highly Sensitive Phenol Biosensor Utilizing Selected Bacillus Biofilm Through an Electrochemical Method". *Makara Journal of Science*. **24** (1): 24–30. 10.7454/mss.v24i1.11726.

[4] K. T. A. Priyangga, Y. S. Kurniawan, L. Yuliati, B. Purwono, T. D. Wahyuningsih, and H. O. Lintang. (2021). "Novel Schiff Base Azo-Imine for Ultra-Sensitive and Highly Selective Fluorescent Chemosensor of Fe^{3+} Ions". *Luminescence: The Journal of Biological and Chemical Luminescence*. 10.1002/bio.4049.

[5] K. T. A. Priyangga, Y. S. Kurniawan, and L. Yuliati. (2021). "Evaluation of *C*-arylcalix[4]resor-cinarenes as Novel Adsorbent Materials: Effect On The Nitro Substituent On The Au(III) Adsorption". *ChemistrySelect*. **6** : 1–9. 10.1002/slct.202101067.

[6] A. W. Czarnik. (2002). In: "J. R. Lakowicz (ed). Topics in Fluorescence Spectroscopy, vol. 4". Springer, Boston, MA. 10.1007/0-306-47060-8_3.

[7] H. Tavallali, G. Deilamy-Rad, A. Parhami, and P. Z. Mousavi. (2013). "A Novel Development of Dithizone as A dual-Analyte Colorimetric Chemosensor: Detection and Determination of Cyanide and Cobalt (II) Ions In Dimethyl Sulfoxide/Water Media With Biological Applications". *Journal of Photochemistry and Photobiology B: Biology*. 125 : 121–130. 10.1016/j.jphotobiol.2013.05.013.

[8] S. M. Saleh, R. Ali, F. Alminderej, and I. A. I. Ali. (2019). "Ultrasensitive Optical Chemosensor for Cu(II) Detection". *International Journal of Analytical Chemistry*. **7381046** : 1–8. 10.1155/2019/7381046.

[9] B. Wang and E. V. Anslyn. (2011). "Chemosensors: Principles, Strategies, and Applications". John Wiley & Sons. 10.1002/9781118019580.

[10] A. M. Costero, M. Parra, S. Gil, and P. Gaviña. (2018). "BODIPY Core as Signaling Unit in Chemosensor Design, BODIPY Dyes – A Privilege Molecular Scaffold with Tunable Properties". *IntechOpen*. 10.5772/intechopen.79591.

[11] R. Martínez-Máñez. (2014). "Virtual Issue: Molecular Sensors". *ChemistryOpen*. **3** : 232–232. 10.1002/open.201402070.

[12] B. Valeur and I. Leray. (2000). "Design Principles of Fluorescent Molecular Sensors for Cation Recognition". *Coordination Chemistry Reviews*. **205** : 3–40. 10.1016/S0010-8545(00)00246-0.

[13] C. H. dos Santos, N. M. Uchiyama, and I. A. Bagatin. (2018). "Selective Azo Dye-Based Colorimetric Chemosensor for F^-, CH_3COO^- and PO_4^{3-}". *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. **210** : 355–361. 10.1016/j.saa.2018.11.057.

[14] L. Yu, Y. Qiao, L. Miao, Y. He, and Y. Zhou. (2018). "Recent Progress in Fluorescent and Colorimetric Sensors for The Detection of Ions and Biomolecules". *Chinese Chemical Letters*. **29** : 1545–1559. 10.1016/j.cclet.2018.09.005.

[15] L. Y. Niu, Y. Z. Chen, H. R. Zheng, L. Z. Wu, C. H. Tung, and Q. Z. Yang. (2015). "Design Strategies of Fluorescent Probes for Selective Detection Among Biothiols". *Chemical Society Reviews*. **44** : 6143–6160. 10.1039/C5CS00152H.

[16] K. T. A. Priyangga, Y. S. Kurniawan, and L. Yuliati. (2020). "Synthesis and Characterizations of C-3-Nitrophenylcalix[4] resorcinarene as A Potential Chemosensor for La(III) Ions". *IOP Conference Series: Material Science and Engineering*. **959** : 012014. 10.1088/1757-899X/959/1/012014.

[17] Y. S. Kurniawan, M. Ryu, R. R. Sathuluri, W. Iwasaki, S. Morisada, H. Kawakita, K. Ohto, M. Maeki, M. Miyazaki, and J. Jumina. (2019). "Separation of Pb(II) Ion with Tetraacetic Acid Derivative of Calix[4]arene by Using Droplet-based Microreactor System". *Indonesian Journal of Chemistry*. **19** : 368–375. 10.22146/ijc.34387.

[18] Y. S. Kurniawan, A. C. Imawan, R. R. Sathuluri, K. Ohto, W. Iwasaki, M. Miyazaki, and J. Jumina. (2019). "Microfluidics Era in Chemistry Field: A Review". *Journal of the Indonesian Chemical Society*, **2** : 7–23. 10.34311/jics.2019.02.1.7.

[19] J. Jumina, H. R. Setiawan, S. Triono, Y. S. Kurniawan, D. Siswanta, A. K. Zulkarnain, and N. Kumar. (2020). "The *C*-Arylcalix[4] pyrogallolarene Sulfonic Acid: A Novel and Efficient Organocatalyst Material for Biodiesel Production". *Bulletin of Chemical Society of Japan*. **93** : 252–259. 10.1246/bcsj.20190275.

[20] J. Jumina, I. Amalina, S. Triono, Y. S. Kurniawan, Y. Priastomo, K. Ohto, and B. M. Yamin. (2021). "Preliminary Application of Organocatalyst Based On *C*-Arylcalix[4]-2-methylresorcinarenes Sulfonic Acid Material for Biodiesel Production". *Bulletin of Korean Chemical Society*. **42** : 403–409. 10.1002/bkcs.12194.

[21] Y. S. Kurniawan, R. R. Sathuluri, K. Ohto, W. Iwasaki, H. Kawakita, S. Morisada, M. Miyazaki, and J. Jumina. (2021). "New Concept for The Study of The Fluid Dynamics of Lithium Extraction Using Calix [4]arene Derivatives in T-Type Microreactor System". *Separations*. **8** : 70. 10.3390/separations8050070.

[22] C. D. Gutsche. (1998). "Calixarene Revisited". The Royal Society of Chemistry. Cambridge. United Kingdom.

[23] B. Mokhtari and K. Pourabdollah. (2013). "Application of Calixarenes in Development of Sensors". *Asian Journal of Chemistry*. **25**:1–12. 10.14233/ajchem.2013.1205.8a.

[24] J. K. Khedkar, M. M. Deshmukh, S. R. Gadre, and S. P. Gejji. (2012). "Hydrogen Bond Energies and Cooperativity in Substituted Calix[n]arenes (n = 4, 5)". *The Journal of Physical Chemistry A*. **116** : 3739−3744. 10.1021/jp3006519.

[25] R. Ludwig. (2000). "Calixarenes in Analytical and Separation Chemistry". *Frensenius' Journal of Analytical Chemistry*. **367** : 103−128. 10.1007/s002160051611.

[26] D. S. Kim and J. L. Sessler (2015). "Calix[4] pyrroles: Versatile Molecular Containers with Ion Transport Recognition, and Molecular Switching Functions". *Chemical Society Reviews*. **44** : 532−546. 10.1039/C4CS00157E.

[27] B. Kaur, N. Kaur, and S. Kumar. (2018). "Colorimetric Metal Ion Sensors-A Comprehensive Review of The Years 2011–2016". *Coordination Chemistry Reviews*. **358** : 13–69. 10.1016/j.ccr.2017.12.002.

[28] K. L. Bicker, S. L. Wiskur, and J. J. Lavigne. (2011). In: "B. Wang, B. Wang, and E. V. Anslyn (eds) Chemosensors". John Wiley & Sons. 275–295. 10.1002/9781118019580.ch14.

[29] D. Wu, A. C. Sedgwick, T. Gunnlaugsson, E. U. Akkaya, J. Yoon, and T. D. James. (2017). "Fluorescent Chemosensors: The Past, Present and Future". *Chemical Society Reviews*. **46**:7105–7123. 10.1039/C7CS00240H.

[30] R. Ali, S. S. Razi, M. Shahid, P. Srivastava, and A. Misra. (2016). "Off – On – Off Fluorescence Behavior of An Intramolecular Charge Transfer Probe Toward Anions and CO_2". *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. **168** : 21–28. 10.1016/j.saa.2016.05.045.

[31] D. Sriramulu and S. Valiyaveettil. (2016). "Perylene Derivatives as A Fluorescent Probe for Sensing of Amines in Solution". *Dyes and Pigments*. **134** : 306–314. 10.1016/j.dyepig.2016.07.028.

[32] Z. Zhang, C. Wang, Z. Zhang, Y. Luo, S. Sun, and G. Zhang. (2018). "Cd(II) Enhanced

Fluorescence and Zn(II) Quenched Fluorescence with Phenylenevinylene Terpyridine: A Theoretical Investigation". *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. **209** : 40–48. 10.1016/j.saa.2018.10.022.

[33] S. Samanta, U. Manna, T. Ray, and G. Das. (2015). "An Aggregation-Induced Emission (AIE) Active Probe for Multiple Targets: A Fluorescent Sensor for Zn^{2+} and Al^{3+} & A Colorimetric Sensor for Cu^{2+} and F⁻". *Dalton Transactions*. **44** : 18902–18910. 10.1039/c5dt03186a.

[34] R. Singh and G. Das. (2018). "Fluorogenic Detection of Hg^{2+} and Ag^{+} Ions Via Two Mechanistically Discrete Signal Genres: A Paradigm of Differentially Responsive Metal Ion Sensing". *Sensors and Actuators B: Chemical*. **258** : 478–483. 10.1016/j.snb.2017.11.097.

[35] G. Fukuhara. (2020). "Analytical Supramolecular Chemistry: Colorimetric and Fluorimetric Chemosensors". *Journal of Photochemistry and Photobiology C: Photochemistry Reviews*. **42** : 100340. 10.1016/j.photochemrev.2020.100340.

[36] Z. Xu, S. Kim, H. N. Kim, S. J. Han, C. Lee, J. S. Kim, X. Qian, and J. Yoon. (2007). "A Naphthalimide–Calixarene as A Two-Faced and Highly Selective Fluorescent Chemosensor for Cu^{2+} or F⁻". *Tetrahedron Letters*. **48** : 9151–9154. 10.1016/j.tetlet.2007.10.109.

[37] K. Wang, D. Guo, B. Jiang, and Y. Liu. (2009). "Highly Selective Fluorescent Chemosensor for Na^{+} Based On Pyrene-Modified Calix[4]arene Derivative". *Science in China Series B: Chemistry*. **52** : 513–517. 10.1007/s11426-009-0011-5

[38] S. K. Dinda, A. Upadhyay, S. Polepalli, M. A. Hussain, and C. P. Rao. (2019). "Development of Nitrobenzoxadiazole-Appended Calix[4]arene Conjugate (L) for Selective Sensing of Trivalent Cr^{3+}, Fe^{3+}, and Al^{3+} Ions in Solution and in The Solid State and Imaging MCF7 Cells by {L + Al^{3+}}". *ACS Omega*. **4** : 7723–7733. 10.1021/acsomega.9b00582.

[39] J. Zhan, F. Fang, D. Tian, and H. Li.

(2012). "Anthraquinone-Modified Calix[4] Arene: Click Synthesis, Selective Calcium Ion Fluorescent Chemosensor and INHIBIT Logic Gate". *Supramolecular Chemistry*. **24** : 272–278. 10.1080/10610278.2012.656124.

[40] J. M. Liu, Q.Y. Zheng, J. L. Yang, C. F. Chen, and Z. T. Huang. (2002). "A New Fluorescent Chemosensor for Fe^{3+} and Cu^{2+} Based On Calix[4]arene". *Tetrahedron Letters*. **43** : 9209–9212. 10.1016/s0040-4039(02)02265-7.

[41] K. -C. Chang, L. -Y. Luo, E. W. -G. Diau, and W. -S. Chung. (2008). "Highly Selective Fluorescent Sensing of Cu^{2+} Ion by An Arylisoxazole Modified Calix[4]arene". *Tetrahedron Letters*. **49** : 5013–5016. 10.1016/j.tetlet.2008.06.060.

[42] G. Arena, F. Attanasio, D. Zhang, Y. Yang, R. A. Bartsch, and C. Sgarlata. (2012). "Selective Sensing of Hg^{2+} by A Proton-Ionizable Calix[4]arene Fluoroionophore". *Analytical and Bioanalytical Chemistry*. **405** : 1133–1137. 10.1007/s00216-012-6378-8.

[43] R. Joseph, J. P. Chinta, and C. P. Rao. (2011). "Calix[4]arene-Based 1,3-Diconjugate of Salicylyl Imine Having Dibenzyl Amine Moiety (L): Synthesis, Characterization, Receptor Properties Toward Fe^{2+}, Cu^{2+}, and Zn^{2+}, Crystal Structures of Its Zn^{2+} and Cu^{2+} Complexes, and Selective Phosphate Sensing by The [ZnL]". *Inorganic Chemistry*. **50** : 7050–7058. 10.1021/ic200544a.

[44] V. V. S. Mummidivarapu, A. Nehra, V. K. Hinge, and C. P. Rao. (2012). "Triazole Linked Picolylimine Conjugate of Calix[6] arene as A Sequential Sensor for La^{3+} Followed by F⁻". *Organic Letters*. **14** : 2968–2971. 10.1021/ol300919h.

[45] M. Kumar, J. N. Babu, V. Bhalla, and R. Kumar. (2010). "Ratiometric/"On–Off" Sensing of Pb^{2+} Ion using Pyrene-appended Calix[4]arenes". *Sensors and Actuators B: Chemical*. **144** : 183–191. 10.1016/j.snb.2009.10.050.

[46] B. Uttam, R. Kandi, M. A. Hussain, and C. P. Rao. (2018). "Fluorescent Lower Rim 1,3-Di-Benzooxadiazole Conjugate of Calix[4]

arene in Selective Sensing of Fluoride in Solution and in Biological Cells Using Confocal Microscopy". *The Journal of Organic Chemistry*. **83** : 11850–11859. 10.1021/acs.joc.8b01761.

[47] R. Hosseinzadeh, F. Maliji, H. Golchoubian, and A. Bekhradnia. (2019). "A Novel Ferrocene-Based Calix[4]arene as An Efficient Optical and Electrochemical Sensor for Highly Selective Fluoride Recognition". *ChemistrySelect*. **4** : 3914–3920. 10.1002/slct.201900241.

[48] H. Gómez-Machuca, C. Quiroga-Campano, C. Jullian, J. D. la Fuente, H. Pessoa-Mahana, C. A. Escobar, J. A. Dobado, and C. Saitz. (2014). "Study by Fluorescence of Calix[4]Arenes Bearing Heterocycles With Anions: Highly Selective Detection of Iodide". *Journal of Inclusion Phenomena and Macrocyclic Chemistry*. **80** : 369–375. 10.1007/s10847-014-0418-2.

[49] S. Memon, A. A. Bhatti, A. A. Bhatti, Ü. Ocak, and M. Ocak. (2015). "Calix[4]arene Based Highly Efficient Fluorescent Sensor for Au^{3+} and I^-". *Journal of Fluorescence*. **25** : 1507–1515. 10.1007/s10895-015-1642-x.

[50] R. Miao, Q. -Y. Zheng, C. -F. Chen, and Z. -T. Huang. (2005). "A Novel Calix[4]Arene Fluorescent Receptor for Selective Recognition of Acetate Anion". *Tetrahedron Letters*. **46** : 2155–2158. 10.1016/j.tetlet.2005.01.138.

[51] H. C. Hung, Y. Y. Chang, L. Luo, C. H. Hung, E. W. G. Diau, and W. S. Chung. (2014). "Different Sensing Modes of Fluoride and Acetate Based On A Calix[4]Arene With 25,27-Bistriazolylmethylpyrenylacetamides". *Photochemical & Photobiological Sciences*. **13** : 370–379. 10.1039/c3pp50175b.

[52] H. M. Chawla, R. Shukla, and P. Goel. (2014). "Sensitive Recognition of Cyanide Through Supramolecularly Complexed New Calix[4]arenes". *New Journal of Chemistry*. **38** : 5264–5267. 10.1039/c4nj00065j.

[53] M. Ramachandran, S. Anandan, and M. Ashokkumar. (2019). "A Luminescent On-Off Probe Based-Calix[4]arene Linked

through Triazole with Ruthenium(II) Polypyridine Complexes to Sense Copper(II) and Sulfide Ions". *New Journal of Chemistry*. **43** : 9832–9842. 10.1039/C9NJ01632E.

[54] H. -F. Xie, C. Wu, J. Zou, Y. -X. Yang, H. Xu, Q. -L. Zhang, C. Redshaw, and T. Yamato. (2020). "A Pyrenyl-appended C-Symmetric Hexahomotrioxacalix[3]arene for Selective Fluorescence Sensing of Iodide". *Dyes and Pigments*. **178** : 108340. 10.1016/j.dyepig.2020.108340.

[55] D. L. Nelson and M. M. Cox. (2017). "Lehninger Principles of Biochemistry (seventh ed.)", Macmillian Higher Education: New York.

[56] P. D. Barata dan J. V. Prata. (2020). "Fluorescent Calix[4]arene-Carbazole-Containing Polymers as Sensors for Nitroaromatic Explosives". *Chemosensors*. **8** : 128. 10.3390/chemosensors8040128.

[57] Y. -W. Xu, L. -L. Tan, J. -M. Liu, L. -M. Xiao, S. -Y. Li, and C. -Y. Su. (2014). "Fluorescent Calix[4]arene Chemosensor for Acidic and Basic Amino Acids In Pure Aqueous Media". *RSC Advances*. **4** : 28046–28051. 10.1039/c4ra04074k.

[58] G. -Y. Qing, F. Wang, Y. -B. He, C. -G. Hu, and X. Yang. (2008). "Highly Selective Fluorescent Recognition of Amino Alcohol Based On Chiral Calix[4]arenes Bearing L-Tryptophan Unit". *Supramolecular Chemistry*. **20** : 635–641. 10.1080/10610270701611204.

[59] R. Zadmard, P. Akbari-Moghaddam, S. Darvishi, and M. Mirza-Aghayan. (2017). "A Highly Selective Fluorescent Chemosensor for NADH Based On Calix[4]arene Dimer". *Tetrahedron*. **73** : 604–607. 10.1016/j.tet.2016.12.053.

[60] M. Panchal, M. Athar, P. C. Jha, A. Kongor, V. Mehta, K. Bhatt, and V. Jain. (2016). "Turn-off Fluorescence Probe for The Selective Determination of Pendimethalin Using a Mechanistic Docking Model of Novel Oxacalix[4]arene". *RSC Advances*. **6** : 53573–53577. 10.1039/C6RA05707A.

[61] X. Zeng, J. Ma, L. Luo, L. Yang, X. Cao, D. Tian, and H. Li. (2015). "Pesticide Macroscopic Recognition by A Naphthol-

Appended Calix[4]arene". *Organic Letters*. **17** : 2976–2979. 10.1021/acs.orglett.5b01075.

[62] C. X. Yu, F. L. Hu, J. G. Song, J. L. Zhang, S. S. Liu, B. X. Wang, H. Meng, L. L. Liu, and L. F. Ma. (2020). "Ultrathin Two-Dimensional Metal-Organic Framework Nanosheets Decorated with Tetra-Pyridyl Calix[4]arene: Design, Synthesis and Application In Pesticide Detection". *Sensors and Actuators B: Chemical*. **310** : 127819. 10.1016/j.snb.2020.127819.