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Research Article

Chemistry for New drug discovery

Design, Synthesis And Evaluation Of New Chemosensors Containing Quinazolinones Moiety For Ions In An Aqueous Medium And Biological Samples

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Abstract: Quinazolinone derivatives were reported as a varied range of biological activity and played a principal part metabolism of all biological systems. The quinazolinone is an organic compound ring containing two merged aromatic rings benzene and pyrimidine. The current project deals with the design and synthesizing new Quinazolinones derivatives and evaluate them as colorimetric chemosensors to detect the cations in the aqueous medium and biological sample. The synthetic strategy depends on acylation of anthranilic acid (1) with butyroyl chloride followed by ring closure to yield benzoxazinone (2), which was reacted with various nucleophiles hydrazine hydrate, urea, thiourea, p-aminophenol, hydroxylamine, and phenyl hydrazine to give corresponding quinazolinone chemosensors 3-amino-2-propylquinazolin-4(3H)-ones (4), 6-nitro-4-oxo-2-propylquinazoline-3(4H)-carboxamide (5a), 6-nitro-4-oxo-2-propylquinazoline-3(4H)-carbothioamide (5b), 3-(2-hydroxyphenyl)-6-nitro-2-propylquinazolin-4(3H)-one (6), 3-hydroxy-2-propylquinazolin-4(3H)-ones (7) and 6-nitro-3-(phenylamino)-2-propylquinazolin-4(3H)-one (8). The importance of producing chemosensors has increased in the last decade. Therefore, here we developed and synthesized chemosensors 4 and 8 with high-selectivity and specificity to detect copper and mercury in both aqueous solutions and blood samples. Where the results showed that chemosesors 4 and 8 exhibited colormetric responses from pale yellow to green in case of Cu^{2+} ions and exhibited remarkable color change from pale yellow to rose by interacting with Hg^{2+}. Chemosensors 5b and 7 show high selectivity toward cadmium ion, whereas chemosensors 5b and 7 exhibited remarkable color change from colorless to yellow when adding Cd^{2+}. but the synthesized compounds 5a and 6 did not exhibit colorimetric response in all cation's samples. In addition, the synthesized chemosensor was established as a strip paper to make the measurement process easy and inexpensive. All the synthesized compounds have been established by instrumental spectroscopy; 1HNMR, 13CNMR, IR, and mass spectra (ms).

Keywords: Chemosensor, Copper, Cadmium, Mercury, Detection, Quinazolinone

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1. INTRODUCTION

Currently, the synthesis of colorimetric sensors and detecting of cations, anions, and toxic ones, is one of the researcher's targets in the organic synthesis field, medical laboratories, environmental, water analysis and biochemistry. [1–6]. In the last decade, several heterocyclic chemosensors were synthesized for the recognition of different ions. [7–10] A few analytical techniques, excluding electrochemical analysis, spectroscopy, amperometric, potentiometric, colorimetric ways, and chromatography were invented to a range of cations and anions from aqueous and non-aqueous situations. [11–15] Cu is the most abundant ion in the human body and many proteins utilize Cu^{2+} as a cofactor for the transfer of electrons in redox reactions. Biologically, excess Cu^{2+} in cells can stimulate the creation of reactive oxygen species, and can harm lipids, DNA and RNA and cause some of the dangerous diseases, such as Dementia's disorder[16] , Prion, Wilson and Menkes disease[17,18], which are directly related to the copper toxicity. In addition, Cu^{2+} is a public cation pollutant because of its wide usage in our daily life. The copper average in drinking water is not more than 1.3 mg/l. [19,20] Fegade. U et al. showed selectivity of dual-channel chemosensor for copper in semi-aqueous media. [21] Kato. T et al., used isotope dilution inductively coupled plasma mass spectrometry for the detection of silver copper, zinc, nickel, lead, and cadmium in seawater[22], Yin. B et al. developed a fluorescence anisotropy assay for the copper ion. [23,24] Lin. W et al. have applied a ratio-metric fluorescent probe for Cu^{2+} determination. [25] There are several detection methods for ions, but colorimetric techniques are the most favorable methods to their low cost, lack of equipment, rapid, and we can detect it by naked eye. [26–28] The development of Cu^{2+} assay by colorimetric chemosensors has much consideration for its toxicity on human fitness. In addition, Cd^{2+} is one of the most ions dispersed in the Earth's crust. It is extremely poisonous to the living organism and its compounds pass in the environment from human activities or geological. Cadmium and its salts are classified as blacklist compounds because high exposure level of cd is associated to raise cardiovascular risks diseases, cancer, liver diseases, and kidney disorder. [29,30] Kim H.N et al. showed a colorimetric and fluorescent sensor for the determination of Cd, Hg, and Pb ions. [31] Li. M et al. utilized a turn-on fluorescent sensor for assay of Cd^{2+}, Hg^{2+}, and Zn^{2+} in water. [32] The interference of Zn^{2+} is one more problem with Cd^{2+} that gives incorrect results after treatment with the sensor.[33] To overcome this problem, Lu et al. [34] designed a sensor containing naphthalimide as the fluorophore, which by undergoing two reverse ICT processes in sensing Zn^{2+} and Cd^{2+} distinguished between this ion pair proficiently. Most reports display the selectivity and sensitivity for the determination of cations and anions in an organic solvent. On the other hand, Mercury is considered the greatest harmful pollutant, which affects directly on human and environmental health, so assay of mercury ions in the environment is a significant target reference. The most reports of sensing Hg^{2+} based on using atomic absorption spectrometry, Raman spectroscopy, inductively coupled plasma mass spectrometry, which is expensive and needs long time pre-treatment. *X.-J. Bai* et al. (2018). Synthesized azo dye-based heterocyclic chemosensors to produce fluorescent sensors for the detection of zinc without interference with cadmium. [35] Ailin Yuan et al. :(2013) synthesis of novel quinazolinone compound as a fluorescence sensor for the ferric ion. [36] Quinazolinone and its derivatives have widespread medical treatments, for instance, antibacterial, anti-fungal, anti-HIV, and antitumor. [37–43] A few reports are utilized to check sensor efficacy. Therefore, producing colorimetric sensors has begun as an important branch and an interesting area of chemistry. In this project, we have synthesized colorimetric chemosensors 4 and 8 that show high selectivity and specificity toward $Cu^{2+}$and Hg^{2+} in aqueous medium and biological samples also, the compounds 5b and 7 showed high selectivity toward Cd^{2+} in aqueous medium and biological sample. While 5a and 6 do not affect all ions. Hence, the significance of producing chemosensors carrying quinazolinone moiety is increasing the selective and specific activity of the sensor. As an extension of our awareness in the Synthesis of heterocyclic compounds, namely pyridopyrimidine[44] and quinazolinone[45], here we synthesize quinazolinone derivatives that have selectivity to react with ions in aqueous and biological samples.

2. MATERIALS AND METHODS

All chemical used in the current research were taken from Marck and Sigma-Aldrich chemical companies, and it were used without further purifications. All melting points are uncorrected and determined by the open capillary method using the Gallen Kamp melting point apparatus. Microanalysis was carried out by the Micro Analytical Unit at Cairo University. IR spectra (KBr disk) were recorded on FT/IR-300E Jasco spectrophotometer. H NMR spectra were recorded in CDCl3 or DMSO-d6 solution on a Varian EM 390-90 MHz.15,16 Mass spectrometry were recorded Shimadzu, GCMS (QP-1000EX).

2.1 *2-butyramide-5-nitrobenzoic acid*

2-amino-5-nitrobenzoic acid (0.1 mol) was allowed to react with n-butyryl chloride 10.5 g (0.11 mol) dropwise in 150 ml of dry pyridine. The mixture was stirred at room temperature (4 hours) and poured into a mixture of ice and hydrochloric acid yielding 89 % crude 2-butyramide benzoic acid crystallized from the methanol. IR(KBr) cm^{-1}: 3431 (OH), 3297(NH), 3040 (CH aromatic), 2966, 2931, 2875 (CH aliphatic), 1697 (C=O, Acid),1669 (C=O, amide); MS: m/z 251 [M+]. Anal. calcd. for C11H11N2O5: C, 52.58; H, 4.38; N, 11.15; O, 31.87. found: C, 52.54; H, 4.39; should be deleted; N, 11.14; O, 31.85.

2.2 *6-nitro-2-propyl-4H-3,1-benzoxazinone*

2-butyramide benzoic acid derivatives (2 g) moistened with acetic anhydride and the mixture was heated for half-hour and then poured in a cold beaker. The obtained solid was recrystallized from petroleum ether giving 6-nitro-2-propyl-4H-3,1-benzoxazinone as a colorless crystals melting point (65 °C). IR(KBr) cm^{-1}: 3061 (CH aromatic), 2971, 2929,2881 (CH aliphatic),1763(C=O), 1616(C=N),1159 (C-O); MS: m/z 234 [M^+], 219, 159, 103. Anal. calcd. for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.70; N, 11.96; please delete. found: C, 56.39; H, 4.67; N, 11.94; O, 27.34.

2.3 3-amino-6-nitro-2-propyl quinazolin-4(3H)-one

Compound (3) (0.01 mol) was heated with 5 ml hydrazine hydrate on a water bath for 1/2 hour, then treated with 50 ml ethanol. The mixture was refluxed 3hours, then concentrated and poured on cooled water, the precipitate formed was collected by filtration, dried and recrystallization from petroleum ether 60- 80 °C to give (75 % yield) **3-**

amino-6-nitro-2-propyl quinazolin-4(3H)-one (4) as a yellow crystals melting point (130 °C). IR(KBr) cm: 3309, 3212 (NH2),3055 (CH aromatic), 2965, 2935, 2875 (CH aliphatic),1673(C=O), 1596(C=N); MS: m/z 248 $[M^+]$, 219, 205, 189, 143, 103. Anal. calcd. for $C_{11}H_{12}N_4O_3$: C, 53.22; H, 4.43; N, 22.58; O, 19.35. found: C, 53.26; H, 4.51; N, 22.64; O, 19.40.

2.4 *6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carboxamide*

Compound 6-nitro-2-propyl-4H-3,1-benzoxazinone (3) (0.0 mol) was treated with urea in boiling glacial acetic acid (50ml) and sodium acetate (0.005 mol) for three hours. The reaction mixture was poured into ice water. The solid was collected by filtration and recrystallized from ethanol affording 6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carboxamide (5a) as a yellow crystals melting point (190 °C). IR(KBr) cm^{-1}: 3325, 3260 (NH2), 3045 (CH aromatic), 2963, 2900, 2862 (CH aliphatic); MS: m/z 276 $[M^+]$, 261, 247, 233, 217, 189, 103. Anal. calcd. for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.34; N, 20.28; O, 23.18. found: C, 52.13; H, 4.31; N, 20.22; O, 23.14.

2.5 *6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carbothioamide*

0.01 Mol of 6-nitro-2-propyl-4H-3,1-benzoxazinone (3) was refluxed with thiourea in glacial acetic acid (50 ml) in the presence of sodium acetate (0.005 mol). The solid product was obtained from pouring the mixture into ice water, and the raw material was filtered and recrystallized from proper solvent ethanol-water (80%-20%) yielding 6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carbothioamide (5b) as a brown crystals melting point (210 °C). IR(KBr) cm^{-1}: 3335, 3280 (NH2), 3045 (CH aromatic), 2963, 2900, 2862 (CH aliphatic), 2265 (C=S), 1650 (C=O), 1605(C=N); MS: m/z 292 $[M^+]$, 277, 263, 249, 233, 189, 103. Anal. Calcd. for $C_{11}H_{10}N_2O_4$: C, 49.31; H, 4.10; N, 19.17; O, 16.43; S, 10.95. found: C, 49.33; H, 4.15; N, 19.13; O, 16.49; S,10.93.

2.6 *3-(2-hydroxyphenyl)-6-nitro-2-propyl quinazolin-4(3H)-one*

(0.01 mol) of 6-nitro-2-propyl-4H-3,1-benzoxazinone (3) was heated under reflux with 4-hydroxy phenylamine (0.01 mol) for 5 hours and completion of the reaction was tested by TLC. The mixture was poured in cold water to yield (65 % yield) 3-(2-hydroxyphenyl)-6-nitro-2-propyl quinazolin-4(3H)-one (6) as a yellow crystals melting point (230 °C). IR(KBr) cm^{-1}: 3542-3377 (OH), 3085 (CH aromatic), 2970, 2915, 2872 (CH aliphatic), 1659(C=O), 1609(C=N); MS: m/z 325 $[M^+]$, 310, 296, 282, 200, 103. Anal. calcd. for $C_{17}H_{15}N_3O_4$: C, 62.77; H, 4.61; N, 12.92; O, 19.69. found: C, 62.82; H, 4.50; N, 12.75; O, 19.75.

2.7 *3-hydroxy-6-nitro-2-propyl quinazolin-4(3H)-one*

A mixture of 6-nitro-2-propyl-4H-3,1-benzoxazinone (10mmol) and hydroxylamine hydrochloride in boiling ethanol (25 ml) was refluxed for 3 hours. The reaction mixture was concentrated and the residue remain was cooled and crystallized from the ethanol to afford 70 % yield of 3-hydroxy-6-nitro-2-propyl quinazolin-4(3H)-one (7) as a pale brown crystals melting point (165 °C). IR(KBr) cm^{-1}: 3415-3290 (OH), 3070 (CH aromatic), 2978, 2905, 2880 (CH aliphatic), 1650(C=O), 1604(C=N); MS: m/z 249 $[M^+]$, 234, 220, 206, 189, 143,103. Anal. calcd. for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.41; N, 16.86; O, 25.70. found: C, 53.08; H, 4.51; N, 16.77; O, 25.77.

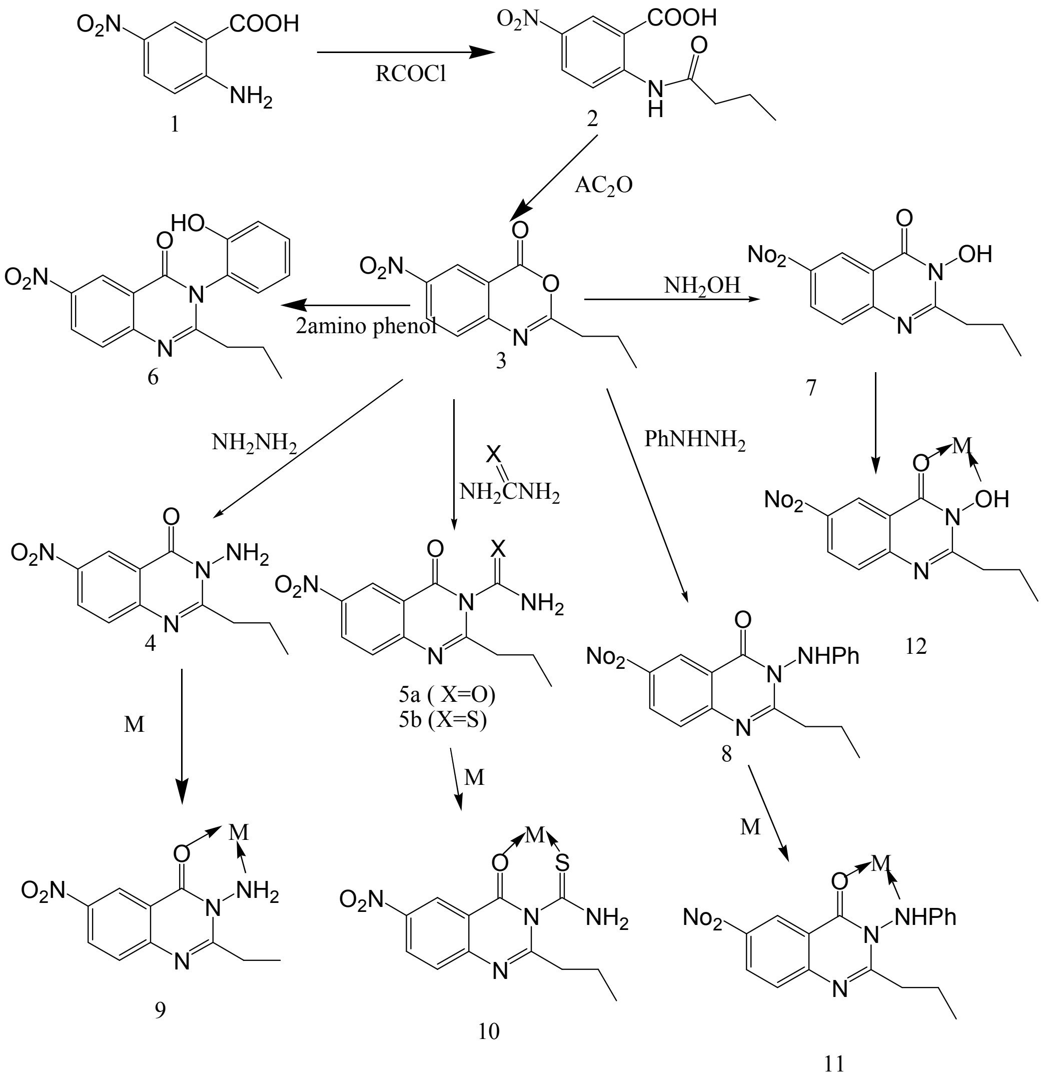
2.8 *6-nitro- 3-(phenylamino)-2-propyl quinazolin-4(3H)-one*

Compound 6-nitro-2-propyl-4H-3,1-benzoxazinone (10 mmol) was treated with phenylhydrazine (20mmol) in ethanol 50 ml under refluxing conditions for three hours, the excess solvent was evaporated, and the residue was poured in water and the produced solid was filtered off and washed with water and recrystallized from the ethanol to give 62 % yield of (8) as a yellow crystals melting point (210 °C). IR(KBr) cm: 3266 (NH), 3067 (CH aromatic), 2955, 2945, 2865 (CH aliphatic),1673(C=O), 1586(C=N); MS: m/z 324 $[M^+]$, 309, 295, 281, 189, 143, 103. Anal. calcd. for $C_{17}H_{16}N_4O_3$: C, 62.96; H, 4.93; N, 17.28; O, 14.81. found: C, 63.00; H, 4.99; N, 17.7257; O, 14.81.

3. RESULTS AND DISCUSSION

3.1 *Synthesize of new chemosensors*

As part of our concern in the organic synthesis of quinazolinone derivatives[45,46], we produced a new chemosensor carrying quinazolinone moiety. As displayed in Scheme 1, anthranilic acid derivative (1) was reacted with butyryl chloride to yield anthanil (2), which was moistened with acetic anhydride giving benzoxazinone (3).[47] The structure of (3) was established from its IR spectra (cm^{-1}) and its microanalytical data, which exhibited strong absorption bands at 1616, 1765 (cm^{-1}) as a result of υ max. of C=N and C=O respectively and the bands for NH and OH were lacked such IR spectrum approved with the planned formula. The benzoxazine (3) was used as a starting material to synthesize quinazolinone chemosensors by the refluxing with various nucleophiles hydrazine hydrate, urea, thiourea, p-aminophenol, hydroxylamine, phenylhydrazine. The reactions products are 3-amino-2-propyl quinazolin-4(3H)-ones (4), 6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carboxamide (5a), 6-nitro-4-oxo-2-propyl quinazoline-3(4H)-carbothioamide (5b), 3-(2-hydroxyphenyl)-6-nitro-2-propyl quinazolin-4(3H)-one (6), 3-hydroxy-2-propyl quinazolin-4(3H)-ones (7) and 6-nitro-3-(phenylamino)-2-propyl quinazolin-4(3H)-one (8) respectively, scheme (1). On the other hand, a sensitivity of all novel quinazolinone derivatives was tested toward different nitrate salts of cations; copper, zinc, manganese, iron, magnesium, manganese, nickel, cobalt, mercury, silver, cadmium, lead, aluminum, potassium, sodium, and calcium.



Scheme. 1Compound 5a; X=O, 5b; X = S. compound 9; M=Cu or Hg , 10; M =Cd, 11; M=Cu or Hg and 12; M=Cd

The FT-IR comparison of chemosensor 4 and its complex 9, chemosensor (5b) and its complex (10), chemosensor (8), and its complex (11) and chemosensor (7) and its complex (12) were identified in the table (1).

Table 1: FT-IR variation between chemosensors and formed complexes.

Chemosensor	Functional group	stretching vibration chemosensor cm^{-1}	stretching vibration complex	Complex
4	(C=O)	1673	1615	9
	(NH_2)	3309 and 3212	3309 and 3190	
5b	(C=O)	1671	1620	10
8	(C=O)	1676	1630	11
	(NH)	3309	3265	
7	(C=O)	1680	1609	12
	(OH)	3325-3530	3290-3403	

The FT-IR spectrum changes of complex (9) confirm primary amine and carbonyl groups are sharing in the binding with metals. Complex (10) confirms carbonyl groups and thiocarbonyl are sharing in the binding with metals (10). Complex (11) suggest carbonyl groups and secondary amine are participating in the binding with metals. (12) suggest the carbonyl groups, hydroxyl groups are participating in the binding metals. The synthesized chemosensors established by elemental analysis, Infrared (IR), Nuclear magnetic resonance (^{1}HNMR, ^{13}CNMR) table 2

Table 2: Nuclear magnetic resonance (^{1}HNMR, ^{13}CNMR) of the synthesized chemosensor.

Chemo-sensor	M.F M.Wt M.P	^{1}HNMR(CDCl3): δ	^{13}CNMR
4	$C_{11}H_{12}N_4O_3$ 248	7.7-8.9 (m, 3H, aromatic),12 (s, 2H, NH_2). 2.2 (t,2H, CH_2Q), 1.9 (sextet,2H, CH_2Me) and	147, 125, 123.3, 153.2, 121.8, 123.7, 155.2, 161, 25.1, 14.6, 13.9

	168-170 °C	1.1(t, 3H, CH_3),	
5a	$C_{12}H_{12}N_4O_4$ 276 152-155 °C	11.5 (s, 2H, NH_2), 7.7-8.8 (m, 3H, aromatic), 2.3 (t,2H, CH_2Q), 1.9 (sextet,2H, CH_2Me) and 0.9(t, 3H, CH_3).	127,133,122.4, 147.1,120,9, 129, 164, 163, 24, 14.9 and 13.9
5b	$C_{12}H_{12}N_4O_3S$ 292 203-205 °C	11.5 (s, 2H, NH_2), 7.6-8.8 (m, 4H, aromatic), 2.3 (t,2H, CH_2Q), 1.9 (sextet,2H, CH_2Me) and 0.9(t, 3H, CH_3),	147,125.8,123.3, 153.2,121.8, 123.7,164,170.6, 27.7, 15.2, 183,13.9
7	$C_{11}H_{11}N_3O_4$ 249 131-133 °C	7.2-8 (m, 4H, aromatic), 3 (s, H, OH), 2.8 (t,2H, CH_2Q),1.8 (sextet,2H, CH_2Me) and 1(t, 3H, CH_3),	127,133,122.4,147.1, 120.9,129, 164, 163 and 24
8	$C_{17}H_{16}N_4O_3$ 324 168-170 °C	12.5 (s, 2H, NH), 7.2-8 (m, 8H, aromatic), 2.8 (t,2H, CH2Q), 1.8 (sextet,2H, CH_2Me) and 1(t, 3H, CH3),	127, 133, 122.4, 147.1, 120.9, 129, 155.2, 161, 25.4, 14.6, 13.9, 151, 113.2, 129.3, 119.2, 129.3 and 113.2

3.2 *Colorimetric study*

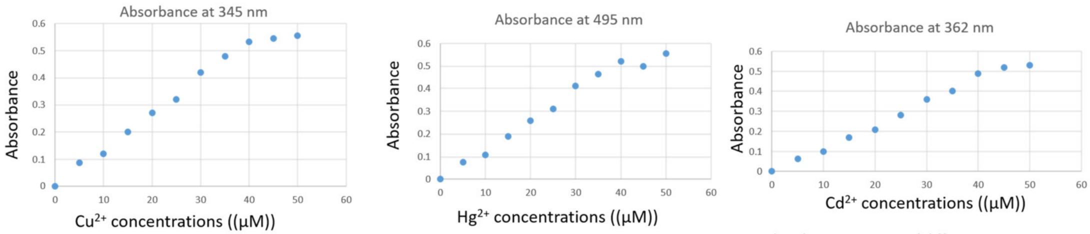
The colorimetric study was applied for 2.5x10^{-5} M of all the synthesized compounds, which were prepared in DMF-water (1:10). As can be seen from table (3), The compounds (5a and 6) did not give any change of color after adding all metals. The chemosensors 4 and 8 exhibited notable color change from pale yellow to green when adding Cu^{2+} ion and the color intensity increased by adding Cu^{2+}. While the chemosensor 4 and 8 exhibited remarkable color change to rose by interacting with $Hg^{2+}$and the intensity of color was increased with adding Hg^{2+}ion. The chemosensor 5b and 7 showed the color change from colorless to yellow when adding Cd^{2+} ion and the intensity of color was increased with the addition of Cd^{2+} ions. This important color change of complex 4, 5b, 7, and 8 can be applied for easily detection Cu^{2+}, Cd^{2+}, and Hg^{2+} ions in an aqueous mediums and biological samples.

Table 3: Colorimetric responses of chemosensor toward various cations

Chemosensor	Detectionion	Colorimetric responses
4	Cu	pale yellow to green
	Hg	pale yellow to rose
5a	All cations	No response
5b	Cd	colorless to yellow
6	All cations	No response
7	Cd	colorless to yellow
8	Cu	pale yellow to green
	Hg	pale yellow to rose

3.3 *UV-VIS absorption spectroscopy study*

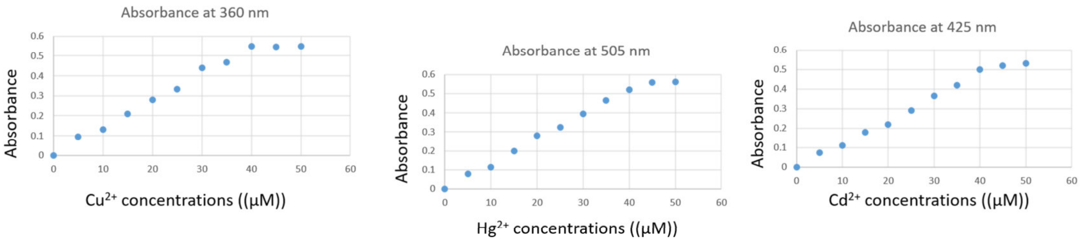
The absorption response of complexes 9, 10,11, and 12 were examined in the presence of different solvents, for instance, ethanol, dimethylformamide, acetonitrile, and. The chemosensor 4, 5b, 7, 8 displayed good absorption intensity in the dimethylformamide solution contrast to other solvents and so we used dimethylformamide as a solvent for all UV-Vis spectral studies because it showed good absorbance shift and absorption intenisty.[48] Metal ions were prepared as Aqueous solutions of 0.02 M nitrate salts in distilled water. Chemosensor stock solutions of 4, 5b,7 and 8 (0.02 M) were dissolved in dimethylformamide. By using a micropipette, we prepared and diluted various concentrations of metal ions to 2.5 x 10^{-5} M with the same solution. The diluted chemosensors were added to various concentrations of metal ions. The complex 9-Cu^{2+} showed the main absorption peak (λ max) at 345 nm. The complex 9-Hg^{2+} showed λ max at 495 nm. The complex 11-Cu^{2+} showed λ max at 360 nm. The complex 11-Hg^{2+} λ max at 505 nm. The complex 10-Cd^{2+} showed λ max at 362 nm, the complex 12-Cd^{2+} displayed λ max at 425 nm. The calibration curves established standard concentrations of ions and specific absorbance for each one fig (1).



Absorbance intensity of different concentration of Cu ion in complex 9-Cu^{2+} at 345 nm

Absorbance intensity of different concentration of Hg ion in complex 9-Hg^{2+} at 495 nm

Absorbance intensity of different concentration of Cd ion in complex 10-Cd^{2+} at 362 nm



Absorbance intensity of different concentration of Cu ion in complex 11-Cu^{2+} at 360 nm

Absorbance intensity of different concentration of Hg ion in complex 11-Hg^{2+} at 505 nm

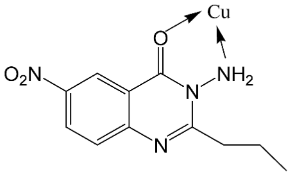
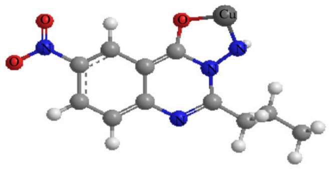
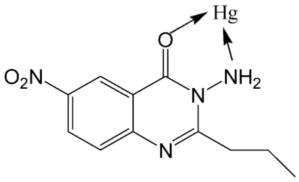
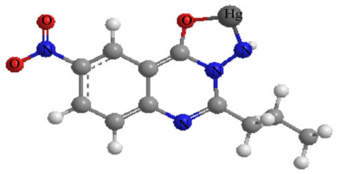
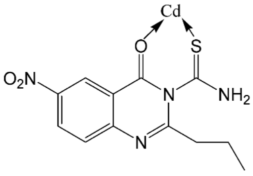
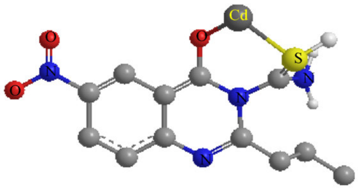
Absorbance intensity of different concentration of Cd ion in complex 12-Cd^{2+} at 425 nm

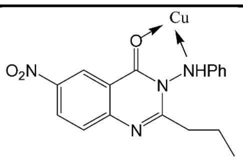
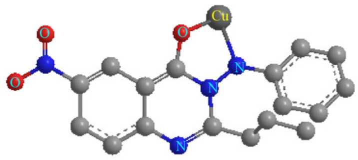
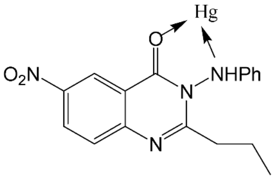
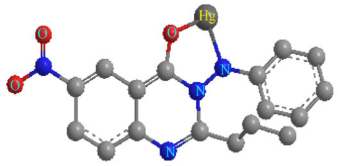
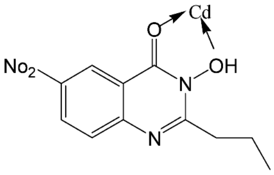
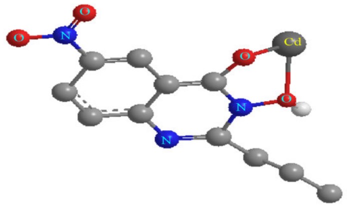
Figure 1: Calibration curves of Absorbance intensity of different concentrations of ions.

3.4 The suggestion mechanism

According to UV-Vis absorption analysis and the FT-IR spectrum of compounds 4, 5b, 7 and 8 and their complexes 9-M^{2+}, 10 M^{2+}, 12 and 11 respectively, the binding positions were labeled in chemosensor 4, 5b, 7 and 8. When compared to the FT-IR spectrum of complexes 9-M^{2+}, 10 M^{2+}, 12 and 11 with that of chemosensors 4, 5b, 7 and 8 table (1), some predictable observations can be inferred. The variations in the FT-IR frequencies of 9 & 11 suggest the primary or secondary amine and carbonyl groups are participating in the binding with metal ions and an established binding mechanism is shown in table (3) Fig. 2, fig 3, fig 5 and fig 6. So, a probable mechanism for the synthesis of complex 9 & 11 is shown in table 3. In the aqueous medium, the nucleophile chemosensor 4&8 attacked cations by lone pairs of electrons from amino and carbonyl groups to form a five-member ring which have high stability and a low amount of ring strained.[49,50] The change of the FT-IR frequencies of complex 10 indicates that Cd^{2+} coordinated with oxygen atom of carbonyl group and C=S group which inform binding mechanism was presented in table (3) Fig. 4. Complex 12 have clearly observed shifts of FT-IR spectrum table (1), which indicated the formation of a binding mechanism is shown in table 3 and in fig.7. The nucleophile chemosensor 8 attacked cations by lone pairs of electrons from OH and C=O groups to form a five-member ring.

Table 3: Proposed binding mechanism of different chemosensors

Chemosensor	λ max	Complex structure	suggested binding mechanism
9-Cu^{2+}	345 nm		 Figure 2
9-Hg^{2+}	495 nm		 Figure 3
10-Cd	362 nm		 Figure 4

11-Cu^{2+}	360 nm		 Figure 5
11-Hg^{2+}	505 nm		 Figure 6
12-Cd^{2+}	425 nm		 Figure 7

3.5 *Application of chemosensor in biological and environmental water samples*

The main purpose of the current study was to detect ions traces in a biological sample, so Samples were collected from the medical laboratory in Al-zulfi hospital. The relationship between absorption and concentration was obtained by the calibration curve and a linear relationship was established to the determination of the concentration of Cu^{2+}, Cd^{2+}, and Hg^{2+} ions in the various blood samples. All blood samples also further assayed by Atomic Absorption Spectroscopy (AAS) to show the chemosensor sensitivity. The synthesized chemosensors 4, 5b, 7, and 8 were carried as strip paper and added one drop of ion analyte to the chemosensor strip which directly detects the concentration of cation.

4. CONCLUSION

The current study established new chemosensors quinazolinones 4 and 8 for the quantitative determination of Cu^{2+}, Cd^{2+} at exact wavelengths in an aqueous medium, and in blood samples. Similarly, chemosensors 5a and 7 have been synthesized for determination of Hg^{2+} ion in an aqueous medium and the environmental samples like water samples. Hence, we designed a paper strip carrying chemosensor, so the determination of Cu^{2+}, Cd^{2+}, and Hg^{2+} will become easy and inexpensive.

5. AUTHOR CONTRIBUTION STATEMENT

Dr. Ayman. M. Algohary designed, prepared, and analyzed the new synthesized compounds. Dr. Esam S. Elmalki evaluated the results and aided to revising of the manuscript and Dr. Sami G. Almalki collected the data, prepared blood samples, and wrote the manuscript. All authors discussed the methodology, results and, contributed to the final manuscript

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7 CONFLICT OF INTEREST

Conflict of interest declared none.

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