DNA binding studies of the 2,10,16,24–tetrakis (phenoxy-3-methoxybenzoic acid)phthalocyaninato) Co(II) and Cu(II) compounds

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Abstract

Tetra phenoxy-3-methoxybenzoic acid substituted Co(II) and Cu(II) metal phthalocyanine compounds were reported for the first time. The structures of these compounds were elucidated by NMR, FT-IR, UV–vis spectroscopy, and elemental analysis. The UV/Vis, fluorescence spectra, viscosity and the thermal melting point techniques were implemented to analyze the DNA bonding activities of cobalt (II) and copper (II) complexes of phthalocyanine by calf thymus DNA. These techniques showed that the phthalocyanine complexes interacted with the DNA molecule through the intercalation mechanism. Additionally, among the methods above, the binding properties of DNA with the compounds **4** and **5** were studied by means of the agarose gel electrophoresis method. The complexes **4** and **5** bonded to the DNA molecule in the buffer system at a pH of 7.02. The findings of these methods proved that the Co(II) and Cu(II) complexes of phthalocyanine could be evaluated as potential cancer medicine for cancer treatment in the near future.

Keywords Aggregation · Synthesis · Absorption spectroscopy · DNA binding · Gel electrophoresis · Phthalocyanine

1 Introduction

Phthalocyanine compounds are utilized in photodynamic healing owing to their high stability, strong electronic absorption ranges and binding to biological molecules [1, 2]. These compounds are substantially large biomolecules and they are used in biological applications as therapeutic medicines and biomarkers [3–8]. Metallic phthalocyanines are critical compounds in terms of treatment and diagnosis practices in different biological, chemical and pharmaceutical processes.

Recently, many people struggle with deadly cancer diseases, and a great number of people die because of cancer [9]. In the literature, studies have shown that cancers are very dangerous medical issues in the world, and it is anticipated that this health problem will continue to cause

the deaths of many people in the future [10]. Therefore, designing of new anticancer drugs is highly important to prevent this deadly disease. Nowadays, there have been very important gains in therapy against this health issue.

Phthalocyanine compounds have a powerful interaction with the DNA molecule [11–17]. DNA binding activity studies with various medicines are significant for finding out the process of binding for drug design [18]. Many therapeutic tiny molecules that tend to bind to the DNA molecules are related to various types of medicines which behave as anticancer medicines and antibiotics [19]. Tiny molecular compounds are prone to bonding to the DNA through the intercalation binding mechanism among the DNA bases. This binding mechanism causes an extension of coiled DNA [20]. In the literature, many studies have reported the interaction of tiny molecules, for instance

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phthalocyanines, actinomycin, daunomycin and epirubicin with the DNA Molecule [16, 21, 22]. Recently, studies showed that various types of cancer medicines bind to the DNA, including the platinum (II) complex [23]. The function of DNA is very important in uncontrolled cell growth in genetic mutation and disorders of repair procedures. Changes and damages in the DNA helix could cause cancer. Therefore, the DNA molecule is the main target for the designing of anticancer drugs [24]. Cancer medicines can interact with the DNA by covalent or noncovalent binding mechanisms [25].

In this study, tetra phenoxy-3-methoxybenzoic acid substituted cobalt (II) (**4**) and copper (II) (**5**) complexes of phthalocyanine were synthesized and characterized by NMR, FT-IR and UV/Vis spectroscopy according a method reported in the literature [26]. The binding activities of the DNA with the complexes **4** and **5** were studied by UV/Vis, fluorescence spectroscopy, thermal melting, gel electrophoresis and viscosity measurements using the DNA in a buffer solution at pH 7.02 at 25 °C.

2 Experimental

2.1 Material and equipment

CoCl₂, CuCl₂, K₂CO₃, 4-hydroxy-3-methoxybenzoic acid, acetone, acetic acid, HCl, methanol, acetonitrile, THF, DMF and DMSO were purchased. Purification and storage were performed according to the methods described in the literature [12]. The melting point was measured electrically by a digital display. A Hitachi U-2900 Spectrophotometer was used for the electronic absorption measurements. The NMR measurements were made by an Agilent 400 MHz spectrometer. A Thermo Scientific FT-IR spectrophotometer was used for the IR analysis.

In this study, the chemical reagents were purchased from the company Sigma. The NaCl, Calf thymus DNA, DMF and Tris-HCl reagents were supplied from commercial companies. The UV/Vis experiments were performed with a Cary 60 UV/Vis spectroscope. The emission titration studies were carried out using a Perkin Elmer LS Fluorescence Spectroscope. A Thermo Scientific Owl Electrophoresis System was used for the agarose gel electrophoresis measurements. The UV/Vis method was applied to measure the thermal melting temperatures, and for the viscosity measurements, an Ubbelohde viscometer apparatus was used. All measurements were conducted in a buffer at a pH of 7.02 at 25 °C.

2.2 The synthesis of the phthalocyanine compounds

2.2.1 4-(3, 4-dicyanophenoxy)-3-methoxybenzoic acid (**3**)

The 4-(3, 4-dicyanophenoxy)-3-methoxybenzoic acid (**3**) compound was synthesized according to a method reported in the literature [26]. A mixture of 4-hydroxy-3-methoxybenzoic acid **1** excess (0.650 g) and 4-nitrophthalonitrile **2** (0.500 g, 2.89 mmol) in 15 mL dimethylsulfoxide (DMSO) was mixed under N₂ at 25 °C. Afterward the first 15 min, the addition of potassium carbonate (2.2 g) to the reaction medium was completed in about 2 h. The reaction process was continued at 25 °C for 48 h. The product was discontinued by spilling the mixture into iced water followed by adjustment of pH to 1.0 with HCl acid and was filtrated and the product was washed up by sufficient pure water. Then, the product was crystallized in ethanol at room temperature. The obtained product dissolves following solvents; acetone, acetonitrile, THF, DMSO and DMF. Yield; 0.54 g (63.5%). mp: 229–231 °C. Anal. Calc. for C₁₆H₁₀N₂O₄: C, 65.31; H, 3.43; N, 9.52; O, 21.75. Found: C, 65.25; H, 3.39; N, 9.49; O, 21.52%. ¹H NMR (400 MHz, DMSO-d₆) δ ppm: 13.17, 8.06, 8.03, 7.74, 7.68, 7.61, 7.31, 7.29 (Ar-H), 3.78(OCH₃), 3.33(DMSO-d₆) 2.48(DMSO-d₆), 1.05 (CH₃). ¹³C NMR (400 MHz, DMSO-d₆): (δ: ppm) 167.02, 161.04, 151.22, 145.17, 136.60, 130.13, 123.37, 122.68, 121.95, 121.33, 117.02, 116.35, 115.82(C≡N), 114.58, 108.54, 56.33, 40.54, 40.34, 40.13, 39.92, 39.71, 39.50, 39.29. FT-IR spectrum (cm⁻¹): 3502, 3084, 2953, 2231, 1680, 1593, 1568, 1500, 1481, 1467, 1425, 1292, 1278, 1261, 1240, 1182, 1159, 1111, 1089, 1018, 952, 873, 842.

2.2.2 The 2,10,16,24-tetrakis (phenoxy-3-methoxybenzoic acid)phthalocyaninato) Co(II)(**4**)

The 2,10,16,24-tetrakis (phenoxy-3-methoxybenzoic acid)phthalocyaninato) Co(II) complex was synthesized according to a procedure reported in the literature [26]. A mixture of 4-(3,4-dicyanophenoxy)-3-methoxybenzoic acid **3** (0.050 g, 0.17 mmol) and CoCl₂ (0.022 g) was powdered in a crucible and heated up in a closed glass tube over 6 min beneath N₂ gaseous at 270 °C. The product was discontinued by spilling the mixture into 2 M HCl (aq) solution followed through staying overnight storage. The precipitated product was filtrated and washed up by pure water and acetic acid solution. Purification was continued by washing in cold and hot methanol. The product dissolved in THF was isolated. The obtained product is soluble in THF, DMSO and DMF solvents. The

yield was 0.020 g (40%). Anal. Calc. for $C_{64}H_{40}N_8O_{16}Co$: C, 62.19; H, 3.26; N, 9.10; O, 20.71; Co, 4.77. Found: C, 62.08; H, 3.22; N, 8.9; O, 20.68; Co, 4.64%. IR spectrum (cm^{-1}): 3523, 3078, 2972, 2900, 1691, 1587, 1463, 1400, 1265, 1217, 1176, 1114, 1093, 1028, 956, 879, 750. UV–Vis (THF) λ_{max} (log ϵ): 662 (5.27), 600(4.81), 326(5.23).

2.2.3 The 2, 10, 16, 24–tetrakis (phenoxy-3-methoxybenzoic acid)phthalocyaninato copper (II) (5)

The 2,10,16,24–tetrakis (phenoxy-3-methoxybenzoic acid) phthalocyaninato Co(II) complex was synthesized according to a method reported in the literature [26]. The synthesis method used for compound **4** was repeated with $CuCl_2$ and with 5 min. The yield was 0.012 g (25%). Anal. Calc. for $C_{64}H_{40}N_8O_{16}Cu$: C, 61.96; H, 3.25; N, 9.03; O, 20.63; Cu, 5.12. Found: C, 61.83; H, 3.17; N, 8.96; O, 20.58; Cu, 5.07%. UV/Vis (THF) λ_{max} (log ϵ): 676 (4.98), 610(4.65), 344(4.88). IR spectrum (cm^{-1}): 3523, 3078, 2972, 2900, 1691, 1598, 1533, 1498, 1404, 1267, 1219, 1178, 1099, 1051, 950, 744.

2.3 DNA binding studies

Tetra phenoxy-3-methoxybenzoic acid substituted Co(II) and Cu(II) phthalocyanine compounds were dissolved in DMF. The calf thymus DNA solutions were set up in a Tris–HCl solution comprising 20 mM Tris–HCl and 20 mM NaCl solution. In order to calculate binding coefficient (K_b) of the compounds **4** and **5**, the experiments were conducted by holding the amounts of compounds fixed while increasing the amounts of the DNA (0–1.5 μM). The K_b constants of the complexes **4** and **5** were calculated with the following equation (F.1) [26].

$$\frac{[DNA]}{(\epsilon a - \epsilon f)} = \frac{[DNA]}{(\epsilon b - \epsilon f)} + \frac{1}{kb(\epsilon b - \epsilon f)} \quad (1)$$

where ϵa , ϵb and ϵf are the electronic spectral constants. The K_b constant was determined from the slope ratio to the intersection. The plot was obtained from $\frac{[DNA]}{(\epsilon b - \epsilon f)}$ versus $[DNA]$.

The emission spectroscopy technique was performed to investigate the binding activity of the compounds **4** and **5** with the CT-DNA. The measurements were conducted by holding the amounts of **4** (15 μM) and **5** (15 μM) constant while increasing the amount of the CT-DNA (0–1.5 μM). The solution consisted of the compounds and the CT-DNA in a buffer solution at a pH of 7.02. Before the experiments, the solution mixture was incubated at the physiological temperature (37 °C) for 5 min. The emission intensity of the compounds interaction with the DNA was observed at 25 °C.

The measurements of the melting temperature point were performed using the electronic absorption technique by observing the absorption spectra of the DNA (25 μM) at 260 nm by increasing the temperature gradually in the absence of the compounds in the buffer solution at a pH of 7.02 [27, 28]. The temperature of the solution was gradually changed from 25 to 105 °C by recording every 5 min. The same procedures were repeated in the presence of the compounds **4** and **5**. The absorption titration spectra were determined by heating the mixture of the CT-DNA and the compounds.

The binding activities of the compounds **4** and **5** with CT-DNA were investigated with the electrophoresis method using the DNA. The CT-DNA interaction experiments were conducted at physiological pH and room temperature. The CT-DNA was treated by differentiating the concentrations of the compounds **4** and **5** in a Tris–HCl at a pH of 7.02. The solutions were incubated at the physiological temperature (37 °C) for 30 min. The solution of the CT-DNA and the compounds solution were loaded by a dye. The gel electrophoresis experiments were recorded at 80 V during 3 h in the buffer solution (TBE) and the bands of the DNA were photographed using a BioRad system. In this method, the measurements were carried out with a Thermo Scientific gel electrophoresis system [29–32].

The viscosity assays were conducted with a viscometer at room temperature (25 °C) in a water bath. The viscometer device was submerged in the water bath at a fixed temperature around 30 °C. The flow time of the samples was recorded three times for each compound. Then, a medial flow time was determined. The viscosity values were derived from the formula $\eta_i = (t_i - t_0)/t_0$, where η_i indicates the viscosity of the calf thymus DNA viscosity, and t_0 shows the buffer flow time at a pH of 7.02. The viscosity values were plotted as $(\eta/\eta_0)^{1/3}$ versus $[compound]/[CT-DNA]$. η represents the viscosity of the DNA in the presence of the compounds **4** and **5**, and η_0 indicates the partial viscosity of the DNA [33].

3 Results and discussion

3.1 Synthesis and characterization of compounds

Synthesis of novel phthalocyanines with different substituents on the periphery and different metals located at the central cavity is still an active area of synthetic inorganic chemistry. Efforts have been ongoing in order to obtain a derivative of phthalocyanines with better and better performance for all application areas. The synthetic route for the synthesis of substituted phthalocyanines from the reaction of novel phthalonitrile derivative (**3**) and phenoxy-3-methoxybenzoic acid is shown in Scheme 1.

Scheme 1 The synthetic path of newly synthesized phthalonitrile derivative (**3**) and phenoxy-3-methoxybenzoic acid substitute phthalocyanine **4** and **5** compounds

Phenoxy-3-methoxybenzoic acid substitute phthalocyanines (**4** and **5**) were synthesized using the reaction among the phthalocyanine compound derivative and metal salts along 5/6 min beneath a N_2 (nitrogen) atmosphere at 270 °C. The new compounds were characterized by using 1H NMR, UV–visible, FT-IR spectra and elemental analysis.

FT-IR spectral data provides information about the vibrations of functional groups. In particular, phthalocyanine complexes are formed on phthalonitrile compounds. In phthalonitrile compounds strong vibrations of CN groups are observed. However, these nitrile peaks disappear as these compounds turn into phthalocyanines. Here, 4-(3,4-dicyanophenoxy)-3-methoxybenzoic acid (**3**) is a phthalonitrile derivative. The absence of the –CN group signals while this compound converts into

phthalocyanines is a sign that the cyclo tetramerization of the phthalocyanine compound occurs.

Figure 1 displays the electronic spectra of **4** in THF at a concentration of $1 \times 10^{-5} \text{ mol.dm}^{-3}$. The Q band for **4** that was observed at 662 nm resulted out of transferring of electrons from the π -HOMO energy state to the π^* -LUMO energy state. The B band resulted out of electronic transitions from a deeper state of the HOMO energy level to the LUMO energy level for the compound **4** that was observed at 326 nm.

Aggregation is the expression of a concept that is seen as non-desired and a problem in some applications. This concept is common in phthalocyanine compounds. It technically limits the application of phthalocyanines. A few of the reasons for which it originates may be listed

Fig. 1 Electronic spectrum of compound **4** in THF

Fig. 2 The change in aggregation for compound **4** with concentration

as concentration, solvents, temperature, substituents and metal ions [13]. In this study, the aggregation process of the compound **4** in the different concentrations of the THF solvent was analyzed by using UV/Vis absorption spectroscopy. The absorption titration spectra of **4** in THF are given in Fig. 2, showing that it did not form aggregates in the THF. Furthermore, the new bands were not monitored because the aggregated species on the compound **4** were unavailable. The Beer-Lambert law was conformed with in the compound at the concentrations as shown in Fig. 2.

The structure of the compound **3** was verified with ^1H NMR on 4-(3,4-dicyanophenoxy)-3-methoxybenzoic acid (**3**) via the protons of the aromatic ring in its relevant regions. In the ^1H NMR spectrum for the compound **3** in the $\text{DMSO}-d_6$ solvent, the aromatic protons come in sight at 13.17 (carboxylic acid), 8.06, 8.03, 7.74, 7.68, 7.61, 7.31, 7.29 (Ar-H), and the aliphatic protons appear at 3.78, 1.05 ppm. In ^{13}C NMR of compound **3**, the new peaks at 116.35 ppm and 115.82 ppm belong nitrile carbons indicated that the substitution occurred between 4-nitrophthalonitrile with 4-hydroxy-3-methoxybenzoic acid groups as shown in Fig. 3a and b. The ^1H NMR spectrum

measurements of **4** and **5** were excluded because of their paramagnetic properties.

3.2 DNA interaction studies

Electronic titration spectra are a very effective technique to study the interaction activities of transition metal complexes by the DNA molecule. In this method, it is well-recognized that variations in the intensity of electronic absorption spectra show the DNA binding mechanism because packing with DNA base pairs harms the DNA's coiled structure [34]. The electronic titration spectra of the compounds **4** and **5** in the absence and the presence of calf thymus DNA at varied amounts were determined as shown in Figs. 3 and 4. The compounds **4** and **5** indicated peak intensities at around 330 nm and 680 nm, respectively, in the buffer at a pH of 7.02. According to reported study in the literature found that DNA binding activity like intercalative interaction mostly is connected with red shift and hypochromicity. Another study in the literature showed that intercalative binding of tiny molecules leads to hyperchromism because of strong packing of aromatic ring to DNA base pairs [10]. Both phthalocyanine compounds indicated hypochromicity, where dropping in absorbance is defined as hypochromicity, and increasing in absorbance is called as hyperchromicity, with the increase in the amounts of the DNA as illustrated in Figs. 4 and 5. The monitored hypochromicity for both compounds demonstrated that the phthalocyanine metal complexes interacted with the CT-DNA by means of the intercalation mechanism. For this reason, the values of the K_b constant were studied to confirm the DNA interaction activities of **4** and **5**. The K_b constant values were found out as 1.85×10^6 and 2.22×10^6 , respectively by using F.1. The obtained K_b values of the compounds **4** and **5** were smaller than the K_b value of ethidium bromide (EB), which is a well-known intercalator compound [35–37], as indicated in Figs. 3 and 4 for the compounds **4** and **5**, respectively. These results proved that the phthalocyanine Co(II) and Cu(II) complexes bound to the CT-DNA using the intercalation binding mechanism [38].

Experiments of the thermal melting point were performed to verify the interaction properties of four phenoxy-3-methoxybenzoic acid substituted the phthalocyanine complexes with the DNA. The thermal melting temperature provides data of the persistence of the double stranded DNA [38]. In the literature, reported a study demonstrated that increase in the thermal melting point values shows the power of binding activity between transition metal and DNA molecule. The melting temperature values could be utilized to specify the binding mechanism of DNA and metal complexes as intercalation or external binding mechanism [1]. In this study,

Fig. 3 **a** The detail of ^1H -NMR spectrum of the compound (3) in the DMSO-d_6 solvent. **b** The ^1H -NMR spectrum of the compound (3) in the DMSO-d_6 solvent

the T_m of calf thymus DNA was obtained as 74.63°C as shown in Fig. 6. Figure 6 shows that the thermal melting temperature differences of the DNA between the compounds **4** and **5** were observed as 79.48°C and 80.75°C ,

respectively. The findings demonstrated that the compounds **4** and **5** interacted with the CT-DNA by means of the intercalation binding mechanism. The findings of the

Fig. 4 The electronic titration spectra of compound **4** upon increasing amount of CT-DNA

Fig. 5 The electronic titration spectra of compound **5** upon increasing amount of CT-DNA

Fig. 6 Thermal denaturation temperatures of CT-DNA (blue) and in the presence of complexes **4** (orange) and **5** (green)

thermal melting studies were compatible with the data on electronic absorption titrations in this study.

Emission titration spectra are a practical technique to investigate the DNA interaction activities of tiny transition

Fig. 7 The Emission titration spectra of the compound **4** in the buffer at a pH of 7.02. The arrow displays the drop in intensities when the concentrations of CT-DNA are gradually increased

metal complexes. The technique provides convenient data over the interaction of metal complexes with the DNA molecule. In the literature, many studies have been reported to explain the binding activities of small compounds with the DNA molecule [39]. A study was reported in literature to determine the binding mechanism by using fluorescence titration method. The result of the study showed that the intensity of emission spectra of DNA considerably decreases in the presence of an intercalative molecule that refers intercalative binding mechanism [10]. Figures 6 and 7 display the emission titration spectra of **4** and **5** in the presence of the DNA in a buffer solution at a pH of 7.02. The arrows illustrate the change in intensities on the increase of the DNA concentrations. When the compounds **4** and **5** were titrated by addition of calf thymus (CT)-DNA, the emission intensities were reduced. The decrease in the intensities showed that **4** and **5** interacted with the CT-DNA via the hypochromic binding mechanism as seen in Figs. 7 and 8 for the compounds **4** and **5**, respectively. These findings verified that the compounds had interaction activities with the CT-DNA using hypochromicity, which means that **4** and **5** interacted with the CT-DNA by the intercalation binding mechanism [40].

Viscosity studies of the DNA interaction activities of **4** and **5** were conducted to confirm the change in the relative viscosities of the DNA by using a viscometer. It is already known that intercalative chemical compounds cause a substantial enhancement in the viscosity of the DNA molecule owing to the extension of the DNA molecule by fitting among DNA base pairs [41]. According to reported study in literature, the findings of study

Fig. 8 The Emission titration spectra of the compound **5** in the buffer at a pH of 7.02. The arrow displays the drop in intensities when the concentrations of CT-DNA are gradually increased

Fig. 9 The relative viscosities of calf thymus DNA (blue) and the relative viscosities of CT-DNA ambience of **4** (red) and **5** (black)

demonstrated that the relative viscosity of DNA scales up as amount of complex increases that is a sign of intercalative binding mechanism [10]. Adversely, the non-intercalative binding mechanisms cause a decrease in the viscosity of DNA [42]. Herewith, the viscosity measurement of the DNA is a considerable procedure to determine the DNA interaction activities of chemical agents [26]. The viscosity experiments of the CT-DNA that were implemented in

the presence of the complexes **4** and **5** are illustrated in Fig. 9. The findings of this method verified that the relative viscosities of the CT-DNA were increased by raising the amounts of the compounds **4** and **5** at a pH of 7.02. The results of the viscosity experiments confirmed that the complexes **4** and **5** interacted with the CT-DNA through the intercalation mechanism.

Additionally, the agarose gel electrophoresis technique was used to analyze the DNA interaction of **4** and **5** at pH 7.02 by using calf thymus DNA for confirmation. The DNA interaction activity of **4** and **5** was monitored by visualization with the gel electrophoresis method. The findings from the gel electrophoresis experiments may be seen in Fig. 9. As shown in Fig. 10, the M lane represents the ladder of the DNA, the C lane belongs to the control DNA and the other lanes belong to the complexes **4** (a) and **5** (b) with different concentrations of the DNA sample. In this technique, the concentrations of the compounds **4** and **5** were kept constant at 20 μ M while the amounts of the DNA ranged from 10 to 20 μ M. The band intensities of the DNA were monitored in the absence of **4** and **5** as indicated in Fig. 10. It was seen that the intensity of the DNA bands was reduced in comparison to the intensity of the C bands. The migration bands of the DNA were partially seen or disappeared due to neutralization of the CT-DNA. The findings of the electrophoresis experiments proved that the complexes **4** and **5** have interaction activities with the CT-DNA.

4 Conclusion

In this present, the phenoxy-3-methoxybenzoic acid substituted Co(II) and Cu(II) phthalocyanine complexes were achieved by a more practical and economical method.

The DNA binding activities of these complexes were studied by using the UV/Vis, emission spectra, thermal melting point, agarose gel electrophoresis and viscosity methods in a buffer solution at a pH of 7.02 at room temperature. Firstly, the binding mechanisms of the compounds were analyzed with electronic spectra, emission spectroscopic methods and thermal melting point profile

Fig. 10 CT-DNA bands of gel electrophoresis for **4** (a) and **5** (b) (20 μ M) in Tris-HCl solution at pH of 7.02 with increasing amounts of the DNA (10–20 μ M). M represents DNA maker and C is the control CT-DNA

studies. The results of these techniques indicated that these phthalocyanine metal complexes interacted with the DNA molecule by intercalation mechanisms. Additionally, electrophoresis and viscosity experiments were performed to analyze the DNA interaction properties for the compounds. The findings of these two methods clearly demonstrated that the phenoxy-3-methoxybenzoic acid substituted Co(II) and Cu(II) complexes bound to the DNA. These results were coherent with the other methods that were used in this study. These findings verified that the compounds **4** and **5** could be promising anticancer compounds because of their DNA interaction activities.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

References

- Ozel A, Barut B, Demirbas Ü, Biyiklioglu Z (2016) Investigation of DNA binding, DNA photocleavage, topoisomerase I inhibition and antioxidant activities of water soluble titanium(IV) phthalocyanine compounds. *J Photochem Photobiol* 157:32–38. <https://doi.org/10.1016/j.jphotobiol.2016.02.005>
- Wang J, Hou Y, Lei W, Zhou Q, Li C, Zhang B, Wang X (2012) DNA photocleavage by a cationic BODIPY dye through both singlet oxygen and hydroxyl radical: new insight into the photodynamic mechanism of BODIPYs. *Chem Phys Phys Chem* 13(11):2739–2747. <https://doi.org/10.1002/cphc.201200224>
- Lebedeva N, Yurina ES, Gubarev YA, Syrbu SA (2018) Interactions of tetracationic porphyrins with DNA and their effects on DNA cleavage. *Spectrochim Acta Part A* 199:235–241. <https://doi.org/10.1016/j.saa.2018.03.066>
- Duprey JLH, Carr-Smith J, Horswell SL, Kowalski J, Tucker JH (2016) Macrocyclic metal complexed DNA conjugates for electrochemical sensing of single nucleobase changes in DNA. *J Am Chem Soc* 138(3):746–749. <https://doi.org/10.1021/jacs.5b11319>
- Ensslen P, Wagenknecht HA (2015) One-dimensional multichromophore arrays based on DNA: from self-assembly to light-harvesting. *Acc Chem Res* 48(10):2724–2733. <https://doi.org/10.1021/acs.accounts.5b00314>
- Mion G, Gianferrara T, Bergamo A, Gasser G, Pierroz V, Rubbiana R, Vilar R, Leczkowska A, Alessio E (2015) Phototoxic activity and DNA interactions of watersoluble porphyrins and their rhenium(I) conjugates. *ChemMedChem* 10:1901–1914. <https://doi.org/10.1002/cmdc.201500288>
- Rangasamy S, Ju H, Um S, Oh DC, Song JM (2015) Mitochondria and DNA targeting of 5,10,15,20-Tetrakis(7-sulfonatobenzo[b] thiophene) porphyrin-induced photodynamic therapy via intrinsic and extrinsic apoptotic cell death. *J Med Chem* 58(17):6864–6874. <https://doi.org/10.1021/acs.jmedchem.5b01095>
- De Oliveira Silva FR, Bellini MH, Nabeshima CT, Schor N, Viera ND, Courrol LC (2011) Enhancement of blood porphyrin emission intensity with aminolevulinic acid administration: a new concept for photodynamic diagnosis of early prostate cancer. *Photodiagn Photodyn Ther* 8:7–13. <https://doi.org/10.1016/j.pdpdt.2010.12.006>
- Siegel RL, Miller KD, Jemal A (2015) Cancer statistics. *CA Cancer J Clin* 65:5–29. <https://doi.org/10.3322/caac.21254>
- Bagda E, Yabaş E, Bagda E (2017) Analytical approaches for clarification of DNA-double decker phthalocyanine binding mechanism: as an alternative anticancer chemotherapeutic. *Spectrochim Acta Part A* 172:199–204. <https://doi.org/10.1016/j.saa.2016.01.019>
- Göksel M, Biyiklioglu Z, Durmuş M (2017) The water soluble axially disubstituted silicon phthalocyanines: photophysical-chemical properties and in vitro studies. *J Biol Inorg Chem* 22(6):953–967. <https://doi.org/10.1007/s00775-017-1473-0>
- Arslan T, Biyiklioglu Z, Şentürk M (2018) The synthesis of axially disubstituted silicon phthalocyanines, their quaternized derivatives and first inhibitory effect on human cytosolic carbonic anhydrase isozymes hCA I and II. *R Soc Chem Adv* 8:10172–10178. <https://doi.org/10.1039/C7RA13674A>
- Barut B, Demirbaş Ü, Şenocak A, Özel A, Kantekin H (2017) Water soluble axially morpholine disubstituted silicon phthalocyanines: synthesis, characterisation, DNA/BSA binding DNA photocleavage properties. *Synth Met* 229:22–32. <https://doi.org/10.1016/j.synthmet.2017.05.006>
- Zheng B, Shen X, Zhao D, Cai Y, Ke M, Huang J (2016) Silicon(IV) phthalocyanines substituted axially with different nucleoside moieties: effects of nucleoside type on the photosensitizing efficiencies and in vitro photodynamic activities. *J Photochem Photobiol B* 159:196–204. <https://doi.org/10.1016/j.jphotobiol.2016.03.055>
- Jiang X, Huang J, Zhu Y, Tang F, Ng D, Sun J (2006) Preparation and in vitro photodynamic activities of novel axially substituted silicon (IV) phthalocyanines and their bovine serum albumin conjugates. *Bioorg Med Chem Lett* 16(9):2450–2453. <https://doi.org/10.1016/j.bmcl.2006.01.075>
- Zhang Y, Lovell J (2017) Recent applications of phthalocyanines and naphthalocyanines for imaging and therapy. *Interdiscip Rev Nanomed NanoBiotechnol* 9(1):1–15. <https://doi.org/10.1002/wnan.1420>
- Song L, Li H, Sunar U, Chen J, Corbin I, Yodh A, Zheng G (2007) Naphthalocyanine-reconstituted LDL nanoparticles for in vivo cancer imaging and treatment. *Int J Nanomed* 2(4):767–774
- Sirajuddin M, Ali S, Badshah A (2013) Drug-DNA interactions and their study by UV-Visible, fluorescence spectroscopies and cyclic voltametry. *J Photochem Photobiol B* 124:1–19. <https://doi.org/10.1016/j.jphotobiol.2013.03.013>
- Rehman SU, Sarwar T, Husain MA, Ishqi HM, Tabish M (2015) Studying non-covalent drug-DNA interactions. *Arch Biochem Biophys* 576:49–60. <https://doi.org/10.1016/j.abb.2015.03.024>
- De Abreu FC, De Paula FS, Ferreira D, Nascimento VB, Lopes JC, Santos A, Santoro MM, Salas CE, Goulart MIO (2008) The application of DNA-biosensors and differential scanning calorimetry to the study of the DNA-binding agent berenil. *Sensors* 8(3):1519–1538. <https://doi.org/10.3390/s8031519>
- Holmlin RE, Stemp ED, Barton JK (1998) Ru(phen)(2)dppz(2+) luminescence: dependence on DNA sequences and groove-binding agents. *Inorg Chem* 37:29–34. <https://doi.org/10.1021/ic970869r>
- Zhou N, James TL, Shafer RH (1989) Binding of actinomycin D to [d(ATCGAT)]₂: NMR evidence of multiple complexes. *Biochemistry* 28(12):5231–5239. <https://doi.org/10.1021/bi00438a047>
- Shahabadi N, Mohammadi S, Alizadeh R (2011) DNA interaction studies of a new platinum(II) complex containing different aromatic dinitrogen ligands. *Bioinorg Chem Appl* 2011:1–8. <https://doi.org/10.1155/2011/429241>

24. Ali A, Bhattacharya S (2014) DNA binders in clinical trials and chemotherapy. *Bioorg Med Chem* 22:4506–4521. <https://doi.org/10.1016/j.bmc.2014.05.030>
25. Baş H, Barut B, Biyiklioglu Z, Özel A (2019) Synthesis, DNA interaction, topoisomerase I, II inhibitory and cytotoxic effects of water soluble silicon (IV) phthalocyanine and naphthalocyanines bearing 1-acetylpiperazine units. *Dyes Pigm* 160:136–144. <https://doi.org/10.1016/j.dyepig.2018.08.005>
26. Fu XB, Wang GT, Liu DD, Lie XY (2014) Synthesis, characterization, DNA binding and cleavage, HSA interaction and cytotoxicity of a new copper(II) complex derived from 2(2'-pyridyl)benzothiazole and glycylglycine. *J Photochem Photobiol A* 276:83–95. <https://doi.org/10.1016/j.jphotochem.2013.12.002>
27. Azza AS, Mohamed MS (2012) DNA-binding, spectroscopic and antimicrobial studies of palladium(II) complexes containing 2,2'-bipyridine and 1-phenylpiperazine. *Spectrochim Acta Part A* 96:586–593. <https://doi.org/10.1016/j.saa.2012.07.012>
28. Apilux A, Tabata O, Chailapakul M (2007) Electrochemical behaviors of native and thermally denatured fish DNA in the presence of cytosine derivatives and porphyrin by cyclic voltammetry using boron-doped diamond electrode. *Bioelectrochemistry* 70:435–439. <https://doi.org/10.1016/j.bioelechem.2006.07.001>
29. Arslantas A, Agirtas MS (2017) Investigation of DNA-binding activities of zinc(II) and cobalt(II) phthalocyanine compounds with 3,4,5-trimethoxybenzyloxy substituents. *ChemistrySelect* 2:11659–11665. <https://doi.org/10.1002/slct.201702362>
30. Reddy PR, Shilpa A, Raju N, Raghavaiah P (2011) Synthesis, structure, DNA binding and cleavage properties of ternary amino acid Schiff base-phen/bipy Cu(II) complexes. *J Inorg Biochem* 105(12):1603–1612. <https://doi.org/10.1016/j.jinorgbio.2011.08.022>
31. Arslantas A, Agirtas MS (2018) Studies on DNA interaction with 2(3),9(10), 16(17), 23(24)-tetrakis 2((4-phenoxyphenyl) diazetylbenzoic acid)phthalocyaninato zinc (II) compound. *ChemistrySelect* 3:1755–1760. <https://doi.org/10.1002/slct.201800172>
32. Liu X-W, Shen YM, Li ZX, Zhong X, Chen YD, Zhang SB (2015) Study on DNA binding behavior and light switch effect of new coumarin-derived Ru(II) complexes. *Spectrochim Acta Part A* 149:150–156. <https://doi.org/10.1016/j.saa.2015.04.063>
33. Cohen G, Eisenberg H (1969) Viscosity and sedimentation study of sonicated DNA–proflavine complexes. *Biopolymers* 8:45. <https://doi.org/10.1002/bip.1969.360080105>
34. Gup R, Erer O, Dilek N (2017) One-pot synthesis of a new 2-substituted 1,2,3-triazole 1-oxide derivative from dipyrindyl ketone and isonitrosoacetophenone hydrazone: nickel(II) complex, DNA binding and cleavage properties. *Bioorg Chem* 71:325–334. <https://doi.org/10.1016/j.bioorg.2017.03.003>
35. Baldini M, Belicchi-Ferrari F, Bisceglie PP, Dall'Aglia G, Pelosi S, Pinelli S, Tarasconi P (2004) Copper(II) complexes with substituted thiosemicarbazones of α -ketoglutaric acid: synthesis, X-ray structures, DNA binding studies, and nuclease and biological activity. *J Inorg Biochem* 43(22):7170–7179. <https://doi.org/10.1021/ic049883b>
36. Zhang QL, Liu JG, Liu J, Xue GQ, Li H, Liu JZ, Zhou H, Qu LH, Ji LN (2001) DNA-binding and photocleavage studies of cobalt(III) mixed-polypyridyl complexes containing 2-(2-chloro-5-nitrophenyl)imidazo [4,5-f][1,10]phenanthroline. *J Inorg Biochem* 85(4):291–296. [https://doi.org/10.1016/S0162-0134\(01\)00212-4](https://doi.org/10.1016/S0162-0134(01)00212-4)
37. Sharma S, Singh SK, Chandra M, Pandey DS (2005) DNA-binding behavior of ruthenium(II) complexes containing both group 15 donors and 2,2':6',2"-terpyridine. *J Inorg Biochem* 99(2):458–466. <https://doi.org/10.1016/j.jinorgbio.2004.10.021>
38. Demirbaş Ü, Barut B, Ozel A, Çelik F, Kantekin H, Sancak K (2019) Synthesis, characterization and DNA interaction properties of the novel peripherally tetra 4-(3-methyl-4-(3-morpholinopropyl)-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl) substituted water soluble Zn(II) and Cu(II) phthalocyanines. *J Mol Struct* 1177:571–578. <https://doi.org/10.1016/j.molstruc.2018.10.006>
39. Zhang SS, Niu SY, Qu B, Jie GB, Xu H, Ding CF (2005) Studies on the interaction mechanism between hexakis(imidazole) manganese(II) terephthalate and DNA and preparation of DNA electrochemical sensor. *J Inorg Biochem* 99(12):2340–2347. <https://doi.org/10.1016/j.jinorgbio.2005.08.016>
40. Özen F, Günel A, Baran A (2018) DNA-binding, enzyme inhibition, and photochemical properties of chalcone-containing metallophthalocyanine compounds. *Bioorg Chem* 81:71–78. <https://doi.org/10.1016/j.bioorg.2018.08.002>
41. Shankaraiah N, Jadala C, Nekkanti S, Senwar KR, Nagesh N, Shrivastava S, Naidu VGM, Sathish M, Kamal A (2016) Design and synthesis of C3-tethered 1,2,3-triazolo- β -carboline derivatives: Anticancer activity, DNA-binding ability, viscosity and molecular modeling studies. *Bioorg Chem* 64:42–50. <https://doi.org/10.1016/j.bioorg.2015.11.005>
42. Saha U, Mukherja K (2014) DNA binding and nuclease activity of an oxovanadium valinato-Schiff base complex. *Int J Biol Macromol* 66:166–171. <https://doi.org/10.1016/j.jbiomac.2014.02.033>

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