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DNA/BSA binding study of iminodiacetate-based gallium(III) complexes

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INTRODUCTION & AIM

Gallium(III) complexes have emerged as promising candidates in bioinorganic chemistry due to their structural versatility, stability, and ability to mimic iron in biological systems, which allows them to interact selectively with key biomolecules. Motivated by these properties, we synthesized two novel gallium(III) complexes, $Na[Ga(ida)_2]\cdot 2H_2O$ (**1**) and $K[Ga(ida)_2]\cdot 3H_2O$ (**2**), employing iminodiacetate (ida^{2-}, **Figure 1**) as the ligand. The synthesis of these complexes was carried out in aqueous solution by reacting $GaCl_3$ with iminodiacetic acid (H_2ida) at 80 °C for 4 h in the presence of NaOH or KOH, respectively. Their structures were determined using IR and NMR (^1H and ^{13}C) spectroscopy and further confirmed through single-crystal X-ray diffraction analysis (**Figure 2**). Building on this structural work, we investigated their interactions with bovine serum albumin (BSA) and calf thymus DNA (ct-DNA) using fluorescence emission spectroscopy to assess their binding affinity towards these biologically important molecules (**Figures 3** and **4**, **Tables 1** and **2**). Since serum albumin consists of three main domains (I–III), each subdivided into two subdomains (A and B), fluorescence competition experiments with site-specific markers were also performed to identify the preferred binding sites of the complexes (**Figure 4**, **Table 2**). Eosin Y served as a marker for site I (subdomain IIA), ibuprofen for site II (subdomain IIIA), and digitoxin for site III (subdomain IB).

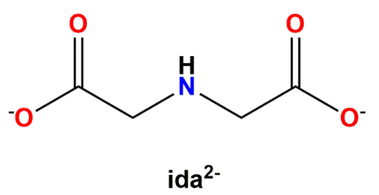

Figure 1. Structural formula of iminodiacetate used for the synthesis of complexes **1** and **2**

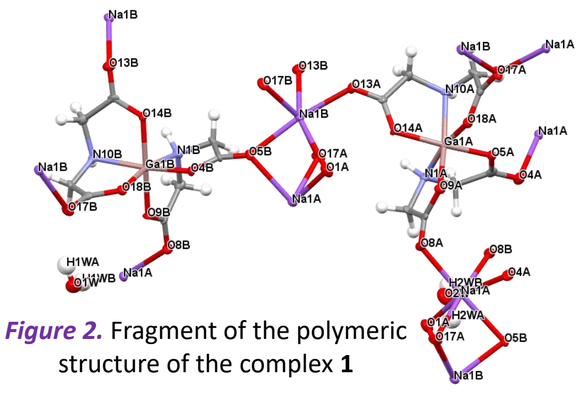

Figure 2. Fragment of the polymeric structure of the complex **1**

METHOD

- Stock solutions of complexes **1** and **2** were prepared in H_2O (1.0×10^{-2} M)
- Their interactions with BSA and ct-DNA were studied using fluorescence emission spectroscopy on a Shimadzu RF-6000 spectrofluorometer

- BSA binding study was performed by tryptophan fluorescence quenching experiments in PBS (pH = 7.4) at room temperature, in the range of 295 – 500 nm, with an excitation wavelength of 290 nm
- The concentration of BSA was constant (4.4 μM), while the concentrations of complexes **1** and **2** were gradually increased (0 – 78.1 μM)

- Competitive binding experiments were performed using the site markers
- Each marker was mixed in equimolar amounts, followed by titration with increasing concentrations of complexes **1** and **2**
- The excitation and emission parameters remained as described before

- DNA binding experiments were also carried out in PBS, by keeping [ct-DNA]/[Hoe] = 10, while increasing the concentrations of complexes **1** and **2** (0 – 160.0 μM)
- Measurements were performed in the wavelength range of 351 – 750 nm, with an excitation wavelength of 346 nm

RESULTS & DISCUSSION

DNA Binding Study

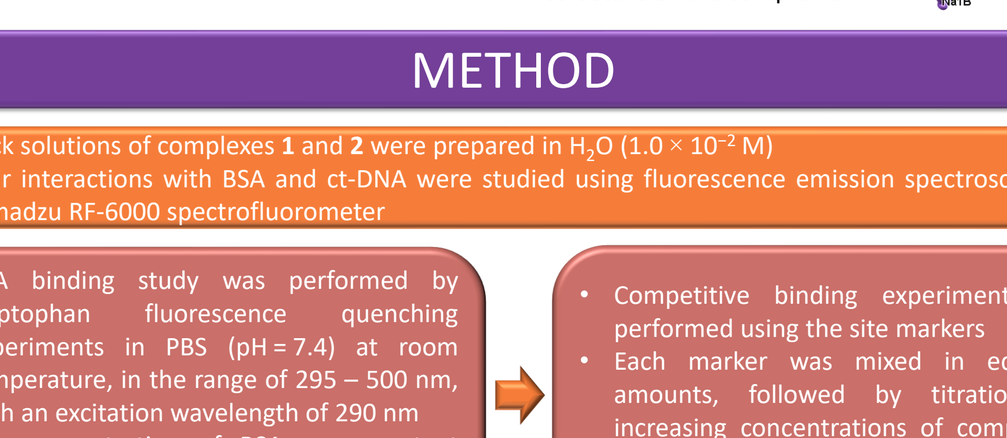

Figure 3. Fluorescence emission spectra for the ct-DNA–Hoe system in the presence of increasing amounts of complex **2**. The red arrow shows the changes of the intensity after the addition of the complex. Inserted graph: Stern-Volmer plot of F_0/F vs. [complex **2**]

Table 1. The values of the binding constants of complexes **1** and **2** with Hoe-ct-DNA system

	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	n
1 – ct-DNA – Hoe	$(3.79 \pm 0.003) \times 10^2$	4.8	3.79×10^{10}	1.15×10^2	0.86
2 – ct-DNA – Hoe	$(3.05 \pm 0.003) \times 10^2$	5.4	3.05×10^{10}	1.60×10^2	0.90

Acknowledgement

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BSA Binding Study and Competitive Experiments with BSA Site Markers

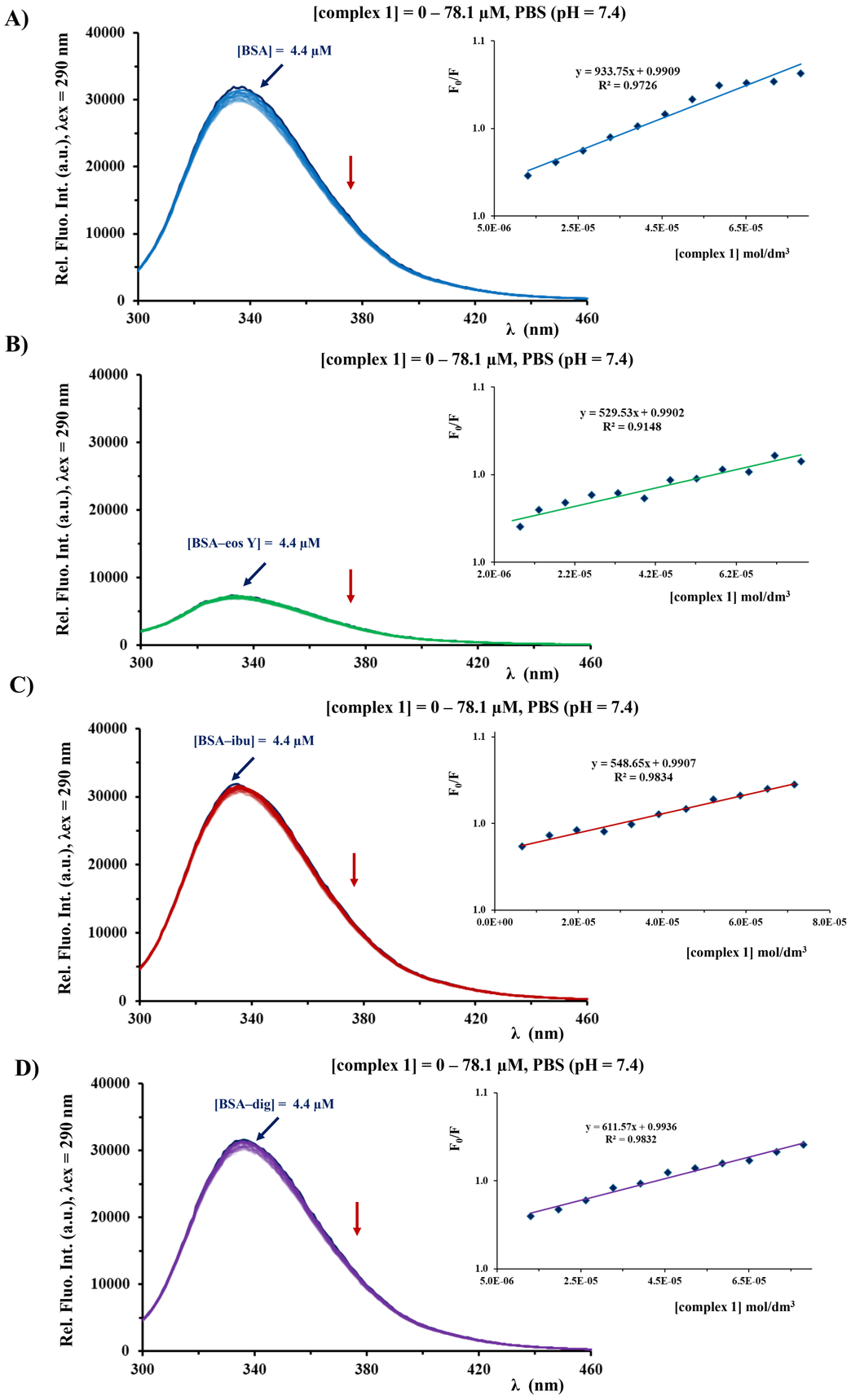

Figure 4. The BSA emission spectra in the presence of an increasing concentration of complex **1** (A) and in presence of the site markers (B – D). The red arrow shows the changes of the intensity after the addition of the complex. Inserted graph: Stern-Volmer plot of F_0/F *vs.* [complex **1**]

Table 2. Values of the BSA binding data for complex **1** in the absence and presence of the site markers, eosin Y (eos Y), ibuprofen (ibu) and digitoxin (dig)

	K_{sv} (M^{-1})	Hypochromism (%)	K_q ($M^{-1}s^{-1}$)	K_A (M^{-1})	n
1 – BSA	$(9.42 \pm 0.003) \times 10^2$	7.3	9.42×10^{10}	1.48×10^3	1.04
1 – BSA – eos Y	$(5.35 \pm 0.001) \times 10^2$	4.4	5.35×10^{10}	4.93×10^2	0.96
1 – BSA – ibu	$(4.34 \pm 0.002) \times 10^2$	3.1	4.34×10^{10}	4.96×10^2	1.01
1 – BSA – dig	$(6.15 \pm 0.001) \times 10^2$	4.6	6.15×10^{10}	9.14×10^2	1.04
2 – BSA	$(8.19 \pm 0.002) \times 10^2$	5.7	8.19×10^{10}	1.34×10^3	1.06
2 – BSA – eos Y	$(7.81 \pm 0.002) \times 10^2$	4.0	7.81×10^{10}	4.43×10^2	0.95
2 – BSA – ibu	$(5.54 \pm 0.001) \times 10^2$	3.9	5.54×10^{10}	2.55×10^2	0.92
2 – BSA – dig	$(6.63 \pm 0.002) \times 10^2$	4.8	6.63×10^{10}	8.96×10^2	1.04

CONCLUSION

- The values of K_A binding constant for complexes **1** and **2** are high enough to indicate their binding to BSA, which can transport these complexes to the corresponding biological targets, but not too high to prevent their release from the BSA upon arrival at the target site
- The largest decrease of the BSA binding constants of complexes **1** and **2** is observed in the presence of eos Y and ibu, indicating that they may compete with these site markers and bind to site I or II of BSA
- Gallium(III) complexes exhibit low binding affinity toward minor groove of ct-DNA

FUTURE WORK / REFERENCES

- Molecular docking studies
- Antimicrobial and cytotoxic evaluation