Electronic Supplementary Material (ESI) for RSC Advances.

Synthesis, characterization, DNA/BSA/HSA interactions, molecular modeling, antibacterial and *in vitro* cytotoxic activities of a novel parent and niosome nano-encapsulated Ho(III) complex

Deng Yinhua [a,b], Mohammad Mehdi Foroughi [c], Zahra Aramesh-Boroujeni [d], Shohreh Jahani [e,*], Mohadesh Peydayesh [f,*], Fariba Borhani [g,*], Mehrdad Khatami [e,h], Meysam Rohani [i], Michal Dusek [j], Vaclav Eigner [j]

[a] *Department of Pharmacy, Hunan Provincial Peoples Hospital, Changsha 410005, PR. China*

[b] *Department of Pharmacy, The First Hospital Affiliated to Hunan Normal University, Changsha 410005, PR. China*

[c] *Department of Chemistry, Kerman Branch, Islamic Azad University, Kerman, Iran*

[d] *Department of Clinical Laboratory, AlZahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran*

[e] *Nanobioelectrochemistry Research Center, Bam University of Medical Sciences, Bam, Iran*

[f] *Clinical Research Center, Pastor Educational Hospital, Bam University of Medical Sciences, Bam, Iran*

[g] *Medical Ethics and Law Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[h] *Cell Therapy and Regenerative Medicine Comprehensive Center, Kerman University of Medical Sciences, Kerman, Iran*

[i] *Department of Medicine, Medical School, Bam University of Medical Sciences, Bam, Iran*

[j] *Institute of Physics of the Czech Academy of Sciences, Na Slovance 2, 18221 Prague 8, Czech Republic*

**Corresponding Author: Tel.: +98 35331321750*

E-mails: shohre_jahani@yahoo.com, drpedayesh57@gmail.com, faribaborhani@msn.com

Table S1. Selected bond lengths (Å) and angles (º) for $[Ho(bpy)(H_2O)_6]Cl_3$

Bond lengths			
X–Y	**X–Y (Å)**	**X–Y**	**X–Y (Å)**
Ho1–O1w	2.317(3)	Ho2–O7w	2.317(3)
Ho1–O2w	2.320(3)	Ho2–O8w	2.332(3)
Ho1–O3w	2.371(3)	Ho2–O9w	2.377(3)
Ho1–O4w	2.326(3)	Ho2–O10w	2.326(3)
Ho1–O5w	2.309(3)	Ho2–O11w	2.302(3)
Ho1–O6w	2.349(3)	Ho2–O12w	2.375(3)
Ho1–N1a	2.492(5)	Ho2–N1b	2.479(5)
Ho1–N2a	2.486(5)	Ho2–N2b	2.492(5)
Bond angles			
X–Y–Z	**X–Y–Z (°)**	**X–Y–Z**	**X–Y–Z (°)**
O1w–Ho1–O2w	74.44(12)	O7w–Ho2–O8w	73.60(12)
O1w–Ho1–O3w	74.65(13)	O7w–Ho2–O9w	73.39(14)
O1w–Ho1–O4w	141.69(13)	O7w–Ho2–O10w	141.25(13)
O1w–Ho1–O5w	98.39(12)	O7w–Ho2–O11w	100.68(13)
O1w–Ho1–O6w	147.00(13)	O7w–Ho2–O12w	147.03(13)
O1w–Ho1–N1a	71.94(13)	O7w–Ho2–N1b	94.01(15)
O1w–Ho1–N2a	96.49(14)	O7w–Ho2–N2b	71.26(13)
O2w–Ho1–O3w	74.55(12)	O8w–Ho2–O9w	75.29(13)
O2w–Ho1–O4w	74.37(11)	O8w–Ho2–O10w	74.52(12)
O2w–Ho1–O6w	128.38(12)	O8w–Ho2–O12w	148.19(12)
O2w–Ho1–N1a	124.77(13)	O8w–Ho2–N1b	75.44(15)
O3w–Ho1–O4w	76.04(12)	O9w–Ho2–O10w	77.69(13)
O4w–Ho1–O5w	96.50(11)	O10w–Ho2–O11w	94.92(12)
O5w–Ho1–O6w	73.58(12)	O11w–Ho2–O12w	73.36(11)
O6w–Ho1–N1a	75.12(12)	O12w–Ho2–N1b	72.15(13)
N1a–Ho1–N2a	65.20(17)	N1b–Ho2–N2b	65.91(17)

Table S2. Hydrogen-bond geometry (Å, °) for the title compound.

D–H···A	D–H (Å)	H···A (Å)	D···H (Å)	D–H···A (°)
O1w–H1o1w···Cl5^{i}	0.82(3)	2.53(4)	3.096(4)	128(4)
O1w–H2o1w···Cl6^{ii}	0.82(3)	2.27(3)	3.060(4)	161(4)
O2w–H1o2w···Cl2^{i}	0.82(3)	2.28(3)	3.084(4)	166(3)
O2w–H2o2w···Cl3	0.820(15)	2.40(2)	3.083(4)	141(3)
O3w–H1o3w···Cl6^{iii}	0.82(3)	2.37(3)	3.154(3)	161(4)
O3w–H2o3w···Cl5^{i}	0.820(14)	2.359(17)	3.110(4)	153(4)
O4w–H1o4w···Cl3	0.82(3)	2.31(3)	3.083(4)	157(4)
O4w–H2o4w···Cl5	0.82(2)	2.31(2)	3.093(3)	161(3)
O5w–H1o5w···Cl6^{iv}	0.82(3)	2.34(3)	3.122(3)	158(3)
O5w–H2o5w···Cl5^{v}	0.82(3)	2.25(3)	3.047(3)	165(3)
O6w–H1o6w···Cl2	0.82(3)	2.27(3)	3.074(4)	167(3)
O6w–H2o6w···Cl6^{iv}	0.82(3)	2.29(3)	3.075(4)	160(3)
O7w–H1o7w···Cl4	0.82(3)	2.58(4)	3.080(4)	121(4)
O7w–H2o7w···Cl1^{vi}	0.82(2)	2.30(3)	3.068(4)	157(3)
O8w–H1o8w···Cl3	0.82(3)	2.29(3)	3.083(4)	161(4)
O8w–H2o8w···Cl2	0.820(11)	2.34(3)	3.086(4)	152(4)
O9w–H1o9w···Cl4	0.82(3)	2.37(2)	3.136(4)	155(4)
O9w–H2o9w···Cl1	0.82(3)	2.34(2)	3.144(3)	167(4)
O10w–H1o10w···Cl2	0.82(2)	2.27(2)	3.077(3)	166(4)
O10w–H2o10w···Cl4^{vii}	0.82(3)	2.27(2)	3.072(4)	166(3)
O11w–H1o11w···Cl1^{viii}	0.82(3)	2.31(3)	3.105(3)	165(3)
O11w–H2o11w···Cl4^{vi}	0.82(3)	2.24(3)	3.057(3)	171(3)
O12w–H2o12w···Cl3^{vii}	0.82(3)	2.31(3)	3.107(4)	165(3)
C3a–H1c3a···Cl1^{iv}	0.96	2.95	3.593(5)	126
C4a–H1c4a···Cl2^{iv}	0.96	2.61	3.532(5)	161
C7a–H1c7a···Cl2^{iv}	0.96	2.88	3.835(8)	177
C9a–H1c9a···Cl4	0.96	2.91	3.612(6)	131
C2b–H1c2b···Cl5	0.96	2.90	3.628(7)	133
C3b–H1c3b···Cl1^{iii}	0.96	2.92	3.879(6)	173
C7b–H1c7b···Cl3^{ix}	0.96	2.61	3.513(5)	157
C8b–H1c8b···Cl6^{vi}	0.96	2.87	3.555(5)	129
C10b–H1c10b···Cl4^{vi}	0.96	2.93	3.888(5)	174

Symmetry codes: (*i*) 1+*x*, *y*, *z*; (*ii*) 2-*x*, 1-*y*, -*z*; (*iii*) *x*, 1+*y*, *z*; (*iv*) 1-*x*, 1-*y*, -*z*; (*v*) 1-*x*, 2-*y*, -*z*; (*vi*) 1-*x*, 1-*y*, 1-*z*; (*vii*) -1+*x*, *y*, *z*; (*viii*) -*x*, 1-*y*, 1-*z*; (*ix*) 1-*x*, 2-*y*, 1-*z*.

Table S3. Energy transfer efficiency E, overlap integral J, the binding distance to tryptophan residue of protein r and Förster critical distance R_0 upon interaction of Ho(III) complex with BSA and HAS ([BSA]=[Ho(III) complex]=1.58 μM, [HSA]=[Ho(III) complex]=2.0 μM, T=298 K and λex=280 nm).

Protein	E	J (cm^3 L mol^{-1})×10^{-13}	R_0 (nm)	r (nm)
BSA	0.20	4.3	2.3	2.7
HSA	0.22	4.5	2.2	2.7

Table S4. Binding energies and inhibition constants of investigated complex for DNA, BSA and HSA binding site.

Macromolecule	Binding Energy (KCal.Mol^{-1})	K_i (μM)
DNA	-5.31	128.14
BSA	-3.67	596.61
HSA	-4.80	304.65

Table S5: The drug concentration causing a 50% reduction in cellular viability (IC50) of the Ho(III) complex and NN-En-Ho against of the MCF-7 and A-549 cell lines.

Cell lines	**The drug concentration causing a 50% reduction in cellular viability (IC50) (µg/ml)**	
	Ho(III) complex	**NN-En-Ho**
MCF-7	**7.23**±0.01	**4.69**±0.02
A-549	**11.45**±0.03	**7.71**±0.01

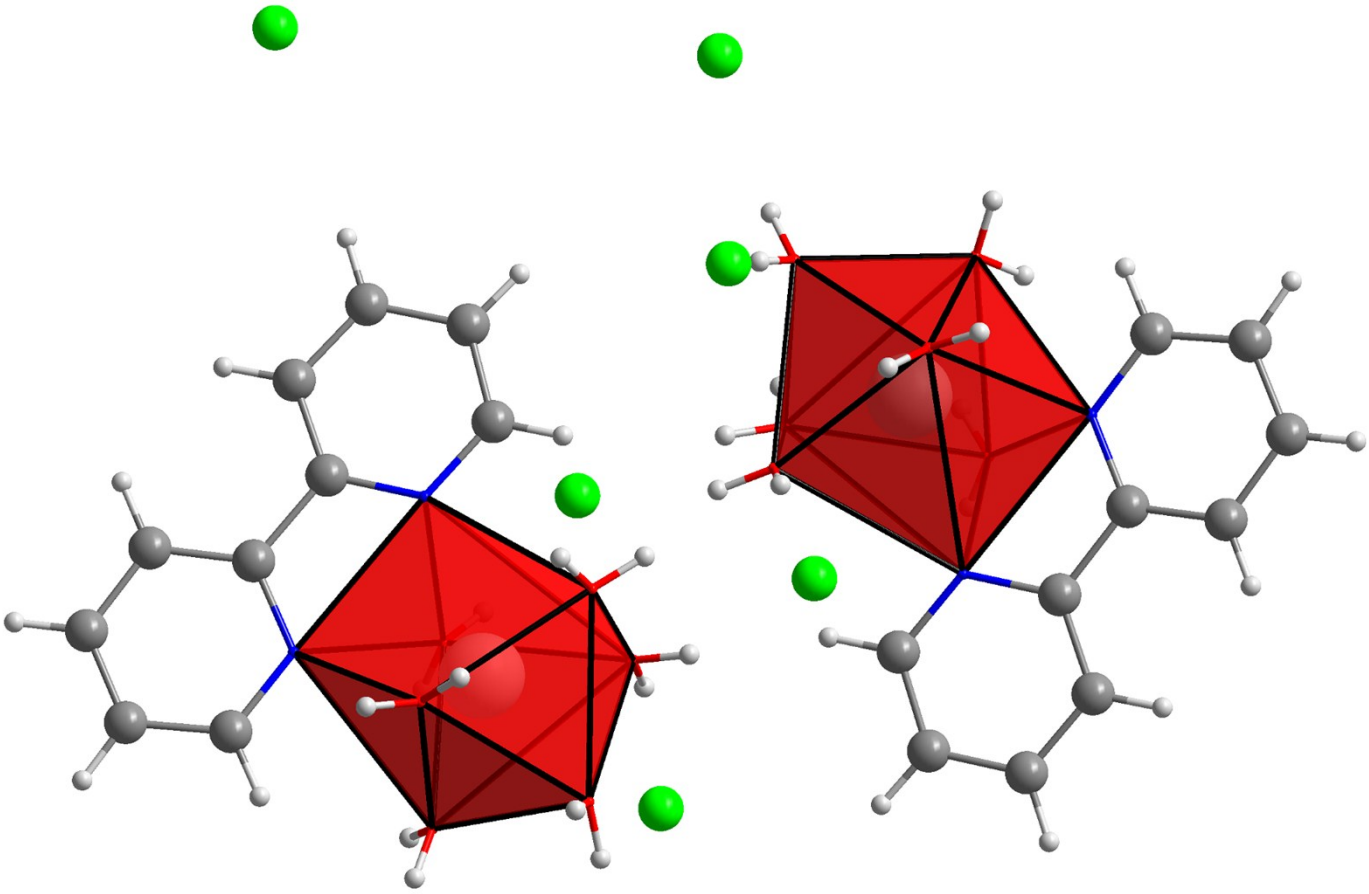

Figure S1. A polyhedral representation of $[Ho(bpy)(H_2O)_6]Cl_3$.

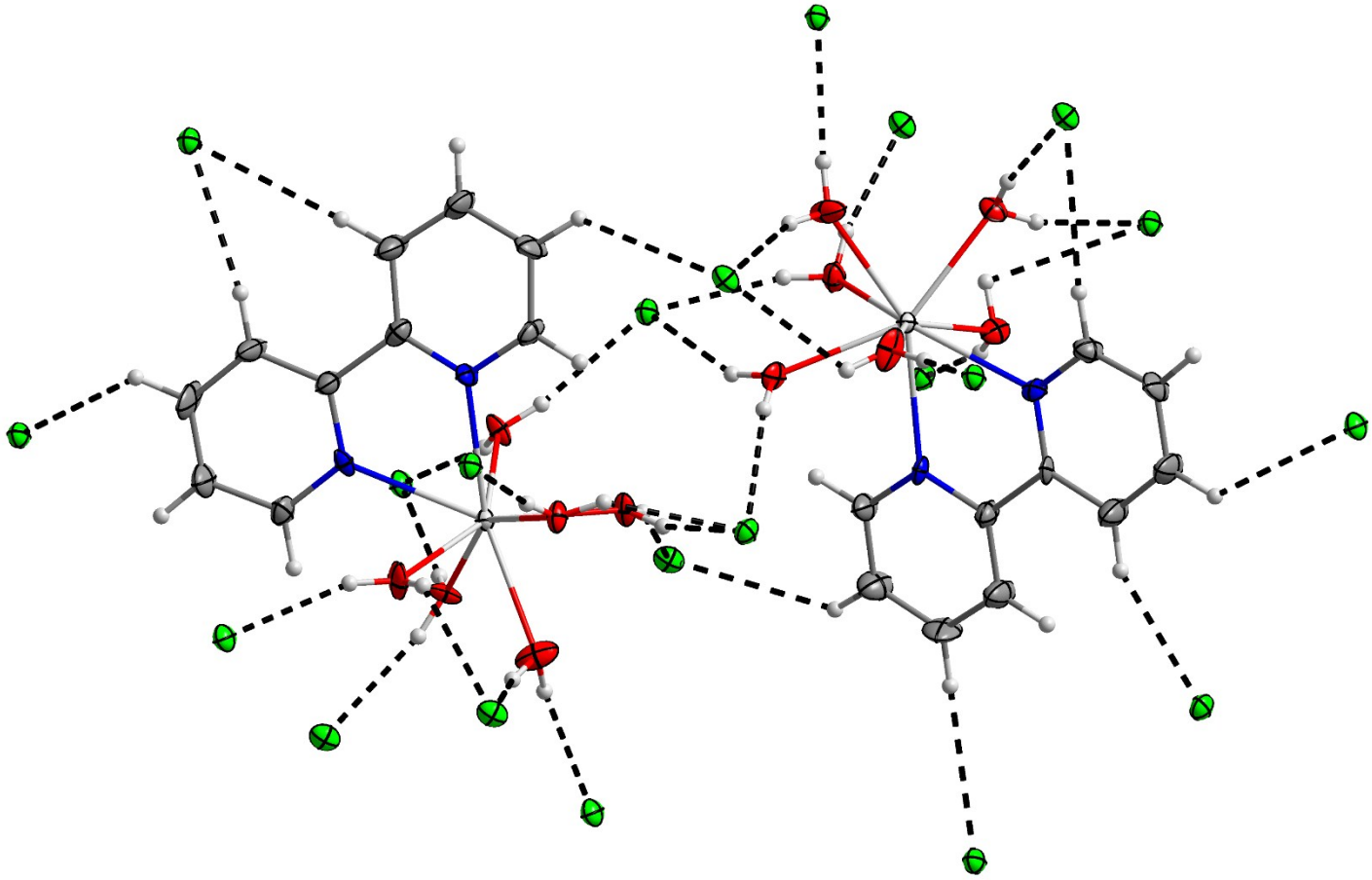

Figure S2. Hydrogen bonds in structure $[Ho(bpy)(H_2O)_6]Cl_3$.

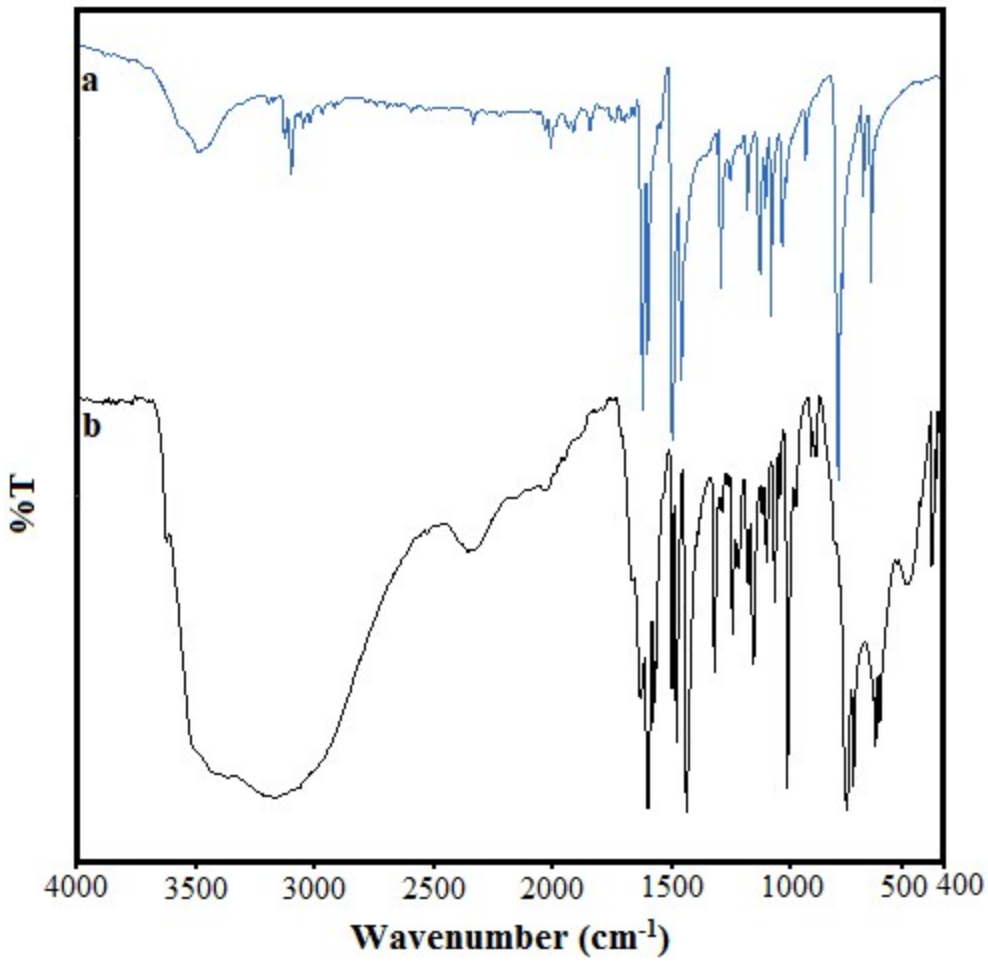

Figure S3. FT-IR spectra of a) bpy, b) $[Ho(bpy)(H_2O)_6]Cl_3$ complex.

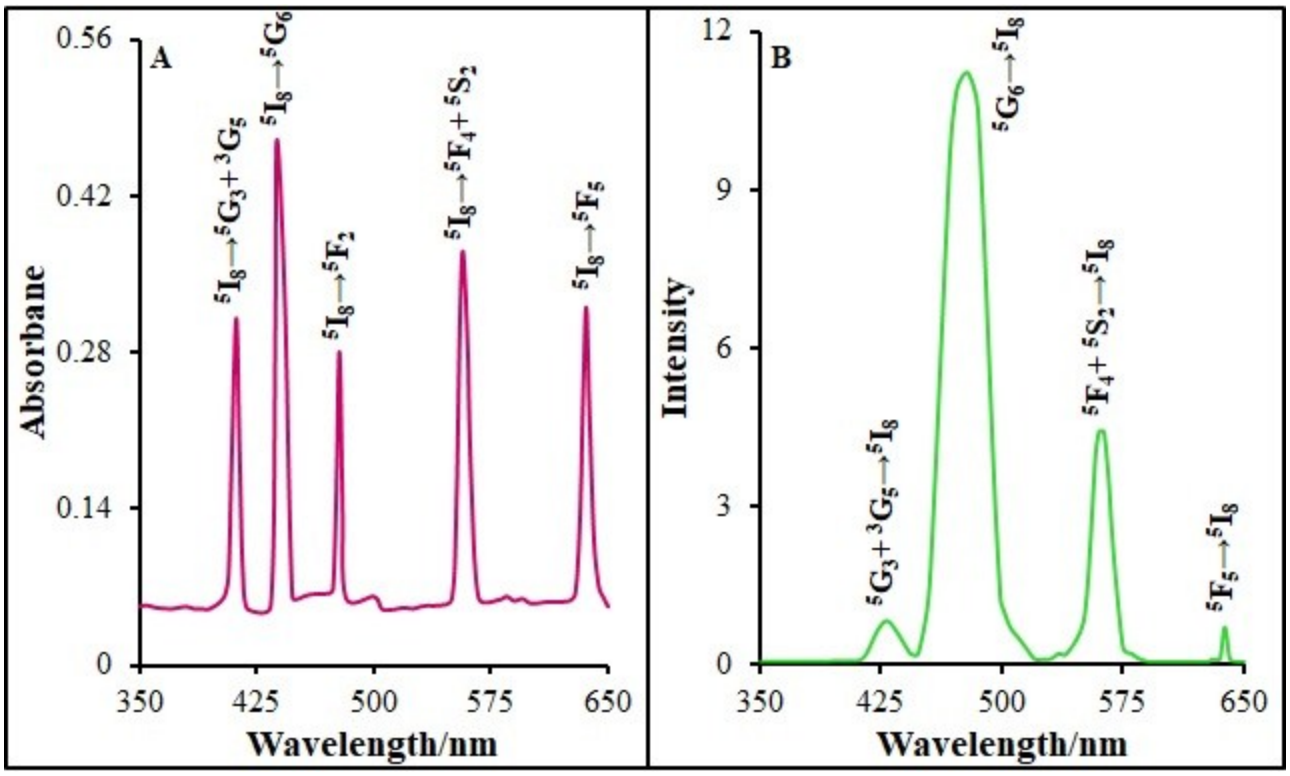

Figure S4. (A) The UV-Vis spectra of the Ho(III) complex in methanol. Ho(III) complex Concentration: 5×10^{-3} M. (B) Emission spectrum of Ho(III) complex λex = 280 nm in methanol at room temperature. Ho(III) complex Concentration: 5×10^{-3} M.

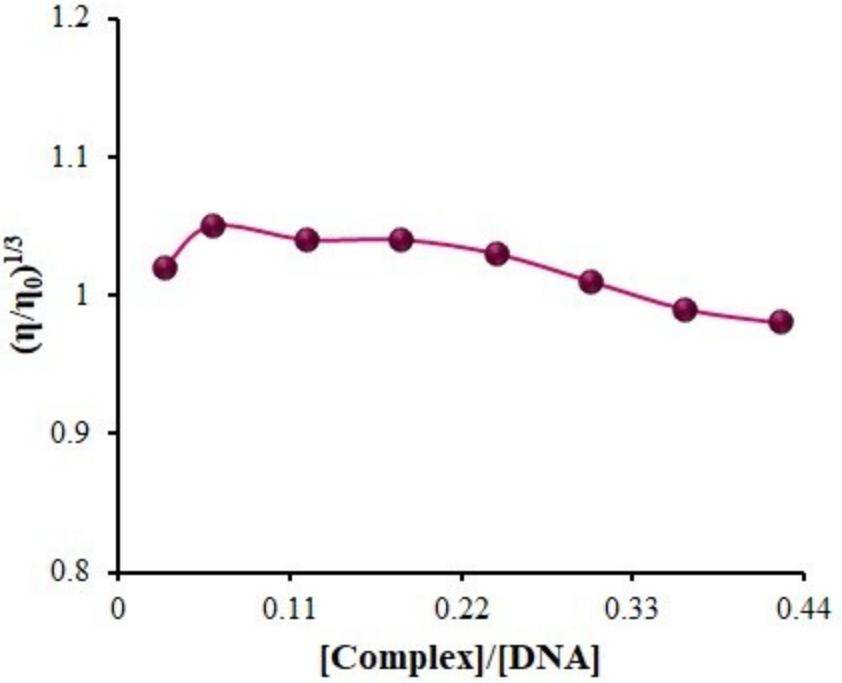

Figure S5. Effect of increasing amounts of Ho(III) complex on the viscosity of FS-DNA in the Tris-HCl buffer solution.