Quinolones and non-steroidal antiinflammatory drugs interacting with copper(II), nickel(II), cobalt(II) and zinc(II) : Structural features, biological evaluation and perspectives

George Psomas* and Dimitris P. Kessissoglou*

Laboratory of Inorganic Chemistry, Faculty of Chemistry, Aristotle University of Thessaloniki, GR-54124 Thessaloniki, Greece.

Supplementary material

* Corresponding authors:

(G. Psomas): Tel.:+30+2310997790; Fax:+30+2310997738; E-mail: gepsomas@chem.auth.gr

(D.P. Kessissoglou): Tel.:+302310997723; Fax:+302310997738; E-mail: kessisog@chem.auth.gr

Table S1. The DNA binding constants (K_b) and Stern-Volmer constants (K_{SV}) of EB-DNA fluorescence for Ni(II)-quinolone complexes.

Compound	**K_b (M^{-1})**	**EB-DNA quenching %**	**$K_{SV(EB-DNA)}$ (M^{-1})**
Hoxo [25d]	3.02(±0.10) x 10^3	---	not determined
[Ni(oxo)$_2$(H$_2$O)$_2$] [25d]	3.11(±0.11) x 10^4	62%	8.56(±0.37) x 10^5
[Ni(oxo)$_2$(bipy)] [25d]	1.43(±0.18) x 10^4	68%	1.20(±0.02) x 10^6
[Ni(oxo)$_2$(phen)] [25d]	2.12(±0.11) x 10^4	60%	8.99(±0.23) x 10^5
[Ni(oxo)$_2$(bipyam)] [25f]	1.41(±0.18) x 10^4	61%	8.91(±0.24) x 10^5
[Ni(oxo)$_2$(py)$_2$] [25d]	1.27(±0.06) x 10^4	80%	8.71(±0.53) x 10^5
Hflmq [25b]	3.53(±0.45) x 10^5	65%	1.19(±0.06) x 10^6
[Ni(flmq)$_2$(H$_2$O)$_2$] [25b]	6.75(±0.55) x 10^5	77%	6.60(±0.40) x 10^5
[Ni(flmq)$_2$(py)$_2$] [25b]	6.36(±0.40) x 10^5	90%	1.30(±0.08) x 10^5
[Ni(flmq)$_2$(4bzpy)$_2$] [25b]	6.81(±0.40) x 10^4	79%	1.54(±0.04) x 10^5
[Ni(flmq)$_2$(bipy)] [25b]	2.82(±0.09) x 10^3	75%	5.90(±0.45) x 10^5
[Ni(flmq)$_2$(phen)] [25b]	5.38(±0.20) x 10^5	55%	2.55(±0.08) x 10^4
[Ni(flmq)$_2$(bipyam)] [25f]	1.05(±0.17) x 10^5	78%	8.85(±0.38) x 10^5
Herx [25e]	1.69(±0.04) x 10^3	36%	1.91(±0.07) x 10^5
[Ni(erx)$_2$(H$_2$O)$_2$] [25e]	1.75(±0.40) x 10^4	78%	5.74(±0.20) x 10^5
[Ni(erx)$_2$(py)$_2$] [25e]	2.59(±0.48) x 10^5	84%	8.38(±0.23) x 10^5
[Ni(erx)$_2$(bipy)] [25e]	4.09(±0.53) x 10^4	86%	1.02(±0.09) x 10^6
[Ni(erx)$_2$(phen)] [25e]	1.63(±0.25) x 10^4	83%	1.03(±0.07) x 10^6
[Ni(erx)$_2$(bipyam)] [25e]	1.73(± 0.21) x 10^3	54%	1.78(±0.12) x 10^5
Hsf [25a]	1.71(±0.02) x 10^5	80%	2.13(±0.09) x 10^6
[Ni(sf)$_2$(H$_2$O)$_2$] [25c]	7.46(±0.17) x 10^5	92%	1.67(±0.10) x 10^6
[Ni(sf)$_2$(py)$_2$] [25a]	3.87(±0.14) x 10^7	81%	2.17(±0.16) x10^6
[Ni(sf)$_2$(bipy)] [25c]	7.75(±0.15) x 10^5	87%	2.31(±0.17) x 10^6
[Ni(sf)$_2$(phen)] [25c]	1.13(±0.18) x 10^6	88%	1.22(±0.07) x 10^6
[Ni(sf)$_2$(bipyam)] [25f]	2.23(±0.25) x 10^4	68%	8.70(±0.34) x 10^5

Table S2. The DNA binding constants (K_b) and Stern-Volmer constants (K_{SV}) of EB-DNA fluorescence for Cu(II)-quinolone complexes.

Compound	**K_b (M^{-1})**	**% of EB-DNA quenching**	Ksv (M^{-1})
Hnorf [26c]	$4.07x10^4$	64%	$8.98x10^5$
Hoflo [26c]	$3.91x10^4$	54%	$4.68x10^5$
[Cu(Hnorf)(phen)Cl]Cl [26c]	$1.83x10^6$	56%	$4.74x10^5$
$[Cu(Hnorf)_2]Cl_2 \cdot 6H_2O$ [26c]	$4.08x10^4$	57%	$3.69x10^5$
$[Cu(Hoflo)_2][(CuCl_2)_2]$ [26c]	$2.56x10^6$	70%	$9.78x10^5$
$[Cu(Hnorf)_2Cl_2] \cdot 2H_2O$ [26c]	$1.97x10^4$	63%	$7.63x10^5$
Hflmq	$3.53x10^5$	65%	$1.19x10^6$
$[Cu(flmq)_2(H_2O)_2]$ [27g]	$8.39x10^3$	68%	$5.50x10^5$
[Cu(flmq)(bipyam)Cl] [27g]	$1.07x10^5$	77%	$6.76x10^5$
[Cu(flmq)(bipy)Cl] [27g]	$1.79x10^5$	74%	$5.42x10^5$
[Cu(flmq)(phen)Cl] [27g]	$2.39x10^5$	77%	$4.32x10^5$
$[Cu(flmq)_2(py)_2]$ [27g]	$8.12x10^5$	78%	$5.42x10^5$

Table S3. The DNA binding constants (K_b) and Stern-Volmer constants (K_{SV}) of EB-DNA fluorescence for Zn(II)-quinolone complexes.

Complex	**K_b (M^{-1})**	**Quenching %**	**K_{SV} (M^{-1})**
Hoxo [30c]	$3.02(\pm0.10) \times 10^3$	---	nd [a]
$[Zn(oxo)_2(H_2O)_2]$ [30c]	$3.12(\pm0.05) \times 10^3$	29%	$1.68(\pm0.01) \times 10^5$
[Zn(oxo)(bipy)Cl] [30c]	$5.91(\pm0.05) \times 10^4$	15%	$1.77(\pm0.15) \times 10^5$
[Zn(oxo)(phen)Cl] [30a]	$1.17(\pm0.09) \times 10^4$	72%	$3.66(\pm0.10) \times 10^5$
$[Zn(oxo)_2(bipy)]$ [30a]	$6.25(\pm0.15) \times 10^4$	79%	$4.60(\pm0.19) \times 10^5$
$[Zn(oxo)_2(phen)]$ [30c]	$9.60(\pm0.02) \times 10^4$	44%	$2.73(\pm0.13) \times 10^5$
$[Zn(oxo)_2(py)_2]$ [31e]	$1.16(\pm0.14) \times 10^5$	85%	$3.68(\pm0.21) \times 10^5$
Hflmq [30b]	$3.53(\pm0.45) \times 10^5$	65%	$1.19(\pm0.06) \times 10^6$
$[Zn(flmq)_2(H_2O)_2]$ [30b]	$7.93(\pm0.23) \times 10^4$	72%	$2.03(\pm0.06) \times 10^5$
[Zn(flmq)(bipy)Cl] [30b]	$2.04(\pm0.26) \times 10^5$	46%	$1.04(\pm0.03) \times 10^5$
[Zn(flmq)(phen)Cl] [30a]	$1.22(\pm0.32) \times 10^6$	52%	$0.59(\pm0.02) \times 10^5$
$[Zn(flmq)_2(bipy)]$ [30b]	$4.71(\pm0.22) \times 10^4$	74%	$0.94(\pm0.05) \times 10^5$
$[Zn(flmq)_2(phen)]$ [30a]	$2.02 (\pm0.21) \times 10^6$	71%	$1.54(\pm0.01) \times 10^5$
Herx [31e]	$1.69(\pm0.04) \times 10^3$	36%	$1.91(\pm0.07) \times 10^5$
$[Zn(erx)_2(H_2O)_2]$ [31f]	$9.32(\pm0.32) \times 10^2$	44%	$2.33(\pm0.09) \times 10^5$
[Zn(erx)(bipy)Cl] [30a]	$1.74(\pm0.11) \times 10^5$	70%	$3.88(\pm0.10) \times 10^5$
[Zn(erx)(phen)Cl] [30a]	$2.68(\pm0.20) \times 10^4$	65%	$3.57(\pm0.11) \times 10^5$
$[Zn(erx)_2(bipy)]$ [31f]	$2.61(\pm0.20) \times 10^4$	65%	$5.88(\pm0.19) \times 10^5$
$[Zn(erx)_2(phen)]$ [31f]	$8.03(\pm0.06) \times 10^4$	60%	$4.31(\pm0.20) \times 10^5$
$[Zn(erx)_2(py)_2]$ [31e]	$3.35(\pm0.05) \times 10^4$	65%	$3.40(\pm0.25) \times 10^5$
Hsf [31a]	$1.71(\pm0.02) \times 10^5$	80%	$2.13(\pm0.09) \times 10^6$
$[Zn(sf)_2(H_2O)_2]$ [31a]	$1.11(\pm0.17) \times 10^4$	80%	$1.29(\pm0.05) \times 10^6$
$[Zn(sf)_2(bipy)]$ [31a]	$1.01(\pm0.06) \times 10^5$	78%	$1.33(\pm0.03) \times 10^6$
$[Zn(sf)_2(phen)]$ [31a]	$2.71(\pm0.22) \times 10^4$	78%	$1.20(\pm0.04) \times 10^6$
$[Zn(sf)_2(bipyam)]$ [31a]	$6.25(\pm0.09) \times 10^5$	72%	$0.99(\pm0.03) \times 10^6$
Hlevo [31a]	$4.36(\pm0.15) \times 10^4$	77%	$1.11(\pm0.03) \times 10^6$
$[Zn(levo)_2(H_2O)_2]$ [31a]	$9.20(\pm0.20) \times 10^3$	77%	$1.16(\pm0.05) \times 10^6$
$[Zn(levo)_2(bipyam)]$ [31a]	$1.08(\pm0.07) \times 10^5$	72%	$1.11(\pm0.03) \times 10^6$

Table S4. The DNA binding constants (K_b) and Stern-Volmer constants (K_{SV}) of EB-DNA fluorescence for Co(II)-NSAID complexes.

Complex	**K_b (M^{-1})**	**EB-DNA quenching**	**K_{SV} (M^{-1})**
Hmef [36a]	$1.05x10^5$	80%	$1.58x10^5$
$[Co(mef)_2(MeOH)_4]$ [36a]	$5.82x10^4$	86%	$7.63x10^5$
$[Co(mef)_2(py)_2(MeOH)_2]$ [36a]	$4.59x10^4$	81%	$1.09x10^6$
$[Co(mef)_2(bipy)(MeOH)_2]$ [36a]	$3.02x10^4$	74%	$4.10x10^5$
$[Co(mef)_2(phen)(MeOH)_2]$ [36a]	$3.22x10^5$	77%	$2.17x10^5$
Hnap [36c]	$2.67x10^4$	82%	$1.47x10^5$
$[Co(nap)_2(MeOH)_4]$ [36c]	$3.15x10^4$	74%	$1.03x10^5$
$[Co(nap)_2(py)_2(H_2O)_2]$ [36c]	$3.58x10^4$	61%	$1.19x10^5$
$[Co(nap)_2(bipy)(H_2O)_2]$ [36c]	$2.76x10^4$	74%	$2.24x10^5$
$[Co(nap)_2(phen)(H_2O)_2]$ [36c]	$2.29x10^4$	83%	$7.17x10^4$
Htolf [36b]	$5.00x10^4$	74%	$1.15x10^6$
$[Co(tolf)_2(MeOH)_4]$ [36b]	$1.14x10^6$	73%	$1.14x10^6$
$[Co(tolf)_2(bipy)(MeOH)_2]$ [36b]	$4.18x10^5$	74%	$1.26x10^6$
$[Co(tolf)_2(phen)(MeOH)_2]$ [36b]	$2.28x10^6$	79%	$1.51x10^6$
$[Co(tolf)_2(bipyam)]$ [36b]	$6.78x10^5$	73%	$1.31x10^6$
$[Co(tolf)_2(py)_2(MeOH)_2]$ [36b]	$9.77x10^5$	78%	$1.41x10^6$

Table S5. The DNA binding constants (K_b) and Stern-Volmer constants (K_{SV}) of EB-DNA fluorescence for Cu(II)-NSAID complexes.

Compound	**K_b (M^{-1})**	**EB-DNA quenching**	**K_{SV} (M^{-1})**
Hnap [38b]	2.67×10^4	82%	1.47×10^5
$[Cu_2(nap)_4(H_2O)_2]$ [38b]	2.27×10^4	80%	1.17×10^5
$[Cu(nap)_2(py)_2(H_2O)]$ [38b]	8.97×10^3	77%	1.88×10^4
$[Cu(nap)_2(bipy)]$ [38b]	3.86×10^4	78%	9.74×10^4
$[Cu(nap)_2(phen)]$ [38b]	9.20×10^3	55%	9.30×10^4
Na dicl [38b]	3.16×10^4	65%	2.47×10^5
$[Cu_2(dicl)_4(H_2O)_2]$ [38b]	1.74×10^4	79%	6.98×10^5
$[Cu(dicl)_2(py)_2]$ [38b]	4.35×10^3	33%	1.35×10^4
$[Cu(dicl)_2(phen)]$ [38b]	1.81×10^4	77%	4.82×10^5
Hmef [38a]	1.05×10^5	80%	1.58×10^5
$[Cu_2(mef)_4(H_2O)_2]$ [38a]	7.59×10^5	71%	1.99×10^5
$[Cu(mef)_2(bipy)]$ [38a]	9.03×10^4	83%	4.72×10^5
$[Cu(mef)_2(phen)]$ [38a]	6.95×10^5	73%	1.04×10^5
$[Cu(mef)_2(bipyam)]$ [38a]	2.20×10^5	82%	2.54×10^6
$[Cu(mef)_2(py)_2(MeOH)_2]$ [38a]	6.93×10^4	88%	1.04×10^6
Hdifl [37b]	3.08×10^3	65%	8.59×10^5
$[Cu_2(difl)_4(DMF)_2]$ [37b]	3.10×10^5	76%	9.03×10^5
$[Cu(difl)_2(py)_2]$ [37b]	7.36×10^4	63%	1.52×10^5
$[Cu(difl)_2(bipy)]$ [37b]	2.97×10^5	64%	4.61×10^5
$[Cu(difl)_2(phen)]$ [37b]	5.61×10^4	69%	6.20×10^5
$[Cu(difl)_2(bipyam)]$ [37b]	8.05×10^4	50%	7.26×10^4

Table S6. The albumins (BSA, HSA) quenching constants (k_q) and association binding constants (K) of Ni(II)-quinolone complexes.

Compound	$\mathbf{k_{q(BSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(BSA)}\ (M^{-1})}$	$\mathbf{k_{q(HSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(HSA)}\ (M^{-1})}$
Hoxo [25d]	5.01×10^{12}	1.09×10^{5}	6.39×10^{12}	1.13×10^{5}
$[Ni(oxo)_2(H_2O)_2]$ [25d]	2.48×10^{12}	9.22×10^{4}	1.76×10^{12}	1.05×10^{4}
$[Ni(oxo)_2(bipy)]$ [25d]	9.85×10^{12}	4.28×10^{4}	6.21×10^{12}	9.07×10^{4}
$[Ni(oxo)_2(phen)]$ [25d]	1.17×10^{13}	6.76×10^{4}	4.07×10^{12}	8.81×10^{4}
$[Ni(oxo)_2(bipyam)]$ [25f]	6.40×10^{12}	4.18×10^{4}	3.01×10^{12}	5.55×10^{4}
$[Ni(oxo)_2(py)_2]$ [25d]	6.86×10^{12}	5.79×10^{4}	2.80×10^{12}	7.21×10^{4}
Hflmq [25b]	8.26×10^{12}	6.67×10^{4}	1.00×10^{13}	2.37×10^{6}
$[Ni(flmq)_2(H_2O)_2]$ [25b]	7.25×10^{12}	7.12×10^{5}	2.04×10^{12}	1.12×10^{6}
$[Ni(flmq)_2(bipy)]$ [25b]	1.24×10^{13}	9.34×10^{4}	3.01×10^{12}	1.25×10^{5}
$[Ni(flmq)_2(phen)]$ [25b]	1.68×10^{13}	8.85×10^{4}	2.36×10^{12}	1.72×10^{5}
$[Ni(flmq)_2(bipyam)]$ [25f]	4.41×10^{13}	2.91×10^{5}	4.22×10^{12}	1.29×10^{5}
$[Ni(flmq)_2(py)_2]$ [25b]	1.62×10^{13}	6.64×10^{4}	1.59×10^{13}	1.84×10^{5}
$[Ni(flmq)_2(4bzpy)_2]$ [25b]	1.84×10^{13}	6.67×10^{4}	4.98×10^{12}	1.19×10^{5}
Herx [25e]	4.40×10^{12}	1.82×10^{4}	3.56×10^{14}	7.63×10^{4}
$[Ni(erx)_2(H_2O)_2]$ [25e]	7.98×10^{12}	5.64×10^{4}	2.27×10^{12}	5.68×10^{4}
$[Ni(erx)_2(phen)]$ [25e]	1.28×10^{13}	1.12×10^{5}	3.77×10^{12}	3.30×10^{4}
$[Ni(erx)_2(bipy)]$ [25e]	1.13×10^{13}	1.03×10^{5}	9.44×10^{12}	8.83×10^{4}
$[Ni(erx)_2(bipyam)]$ [25f]	1.28×10^{13}	1.12×10^{5}	1.72×10^{12}	8.58×10^{4}
$[Ni(erx)_2(py)_2]$ [25e]	7.71×10^{12}	7.51×10^{4}	2.96×10^{12}	9.43×10^{4}
Hsf [25a]	1.04×10^{13}	7.30×10^{4}	1.26×10^{13}	6.00×10^{4}
$[Ni(sf)_2(H_2O)_2]$ [25c]	4.06×10^{13}	1.91×10^{5}	1.84×10^{13}	6.79×10^{4}
$[Ni(sf)_2(phen)]$ [25c]	4.77×10^{13}	2.55×10^{4}	1.41×10^{13}	9.20×10^{6}
$[Ni(sf)_2(bipy)]$ [25c]	2.25×10^{13}	1.00×10^{5}	2.17×10^{13}	4.50×10^{4}
$[Ni(sf)_2(bipyam)]$ [25f]	3.62×10^{13}	4.18×10^{4}	1.14×10^{13}	4.43×10^{4}
$[Ni(sf)_2(py)_2]$ [25a]	3.92×10^{13}	4.10×10^{4}	1.80×10^{13}	1.00×10^{5}

Table S7. The albumins (BSA, HSA) quenching constants (k_q) and association binding constants (K) of Cu(II)-quinolone complexes.

Compound	$\mathbf{k_{q(BSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(BSA)}\ (M^{-1})}$	$\mathbf{k_{q(HSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(HSA)}\ (M^{-1})}$
Hnorf [26c]	8.09×10^{12}	1.73×10^{4}	4.90×10^{12}	7.20×10^{5}
Hoflo [26c]	1.07×10^{13}	5.88×10^{4}	2.99×10^{12}	2.73×10^{4}
[Cu(Hnorf)(phen)Cl]Cl [26c]	1.92×10^{13}	7.09×10^{4}	5.45×10^{12}	4.22×10^{4}
$[Cu(Hnorf)_2]Cl_2\cdot6H_2O$ [26c]	5.35×10^{12}	6.16×10^{4}	5.19×10^{12}	8.84×10^{4}
$[Cu(Hoflo)_2][(CuCl_2)_2]$ [26c]	1.92×10^{13}	4.51×10^{4}	5.91×10^{12}	4.51×10^{4}
$[Cu(Hnorf)_2Cl_2]\cdot2H_2O$ [26c]	1.39×10^{13}	5.56×10^{4}	6.48×10^{12}	4.27×10^{4}
Hflmq [27g]	8.26×10^{12}	6.67×10^{4}	1.00×10^{13}	2.37×10^{6}
$[Cu(flmq)_2(H_2O)_2]$ [27g]	1.35×10^{13}	4.29×10^{4}	5.28×10^{12}	7.55×10^{4}
[Cu(flmq)(bipyam)Cl] [27g]	8.04×10^{12}	2.62×10^{5}	5.28×10^{12}	1.58×10^{5}
[Cu(flmq)(bipy)Cl] [27g]	7.84×10^{12}	1.14×10^{5}	2.68×10^{12}	1.26×10^{5}
[Cu(flmq)(phen)Cl] [27g]	2.25×10^{13}	3.24×10^{5}	2.51×10^{12}	1.28×10^{5}
$[Cu(flmq)_2(py)_2]$ [27g]	7.85×10^{12}	1.20×10^{5}	2.04×10^{12}	1.27×10^{5}

Table S8. The albumins (BSA, HSA) quenching constants (k_q) and association binding constants (K) of Zn(II)-quinolone complexes.

Compound	$k_{q(BSA)}$ **($M^{-1} s^{-1}$)**	$K_{(BSA)}$ **(M^{-1})**	$k_{q(HSA)}$ **($M^{-1} s^{-1}$)**	$K_{(HSA)}$ **(M^{-1})**
Hoxo [30c]	$5.01x10^{12}$	$1.09x10^{5}$	$6.39x10^{12}$	$1.13x10^{5}$
$[Zn(oxo)_2(H_2O)_2]$ [30c]	$7.20x10^{12}$	$7.11x10^{4}$	$3.62x10^{12}$	$8.83x10^{4}$
[Zn(oxo)(bipy)Cl] [30c]	$3.35x10^{12}$	$1.46x10^{5}$	$3.46x10^{12}$	$1.78x10^{5}$
[Zn(oxo)(phen)Cl] [30a]	$8.96x10^{12}$	$2.10x10^{5}$	$2.35x10^{12}$	$5.85x10^{4}$
$[Zn(oxo)_2(bipy)]$ [30a]	$1.89x10^{13}$	$1.62x10^{5}$	$7.69x10^{12}$	$1.73x10^{5}$
$[Zn(oxo)_2(phen)]$ [30c]	$6.37x10^{12}$	$3.36x10^{4}$	$3.14x10^{12}$	$3.09x10^{4}$
Hflmq [30b]	$8.26x10^{12}$	$6.67x10^{4}$	$1.00x10^{13}$	$2.37x10^{6}$
$[Zn(flmq)_2(H_2O)_2]$ [30b]	$1.07x10^{13}$	$5.60x10^{4}$	$2.91x10^{12}$	$9.59x10^{4}$
[Zn(flmq)(bipy)Cl] [30b]	$5.28x10^{12}$	$8.40x10^{4}$	$2.68x10^{12}$	$1.26x10^{4}$
[Zn(flmq)(phen)Cl] [30a]	$4.45x10^{12}$	$4.83x10^{4}$	$4.30x10^{12}$	$6.51x10^{4}$
$[Zn(flmq)_2(bipy)]$ [30b]	$1.68x10^{12}$	$1.68x10^{4}$	$1.83x10^{12}$	$7.91x10^{4}$
$[Zn(flmq)_2(phen)]$ [30a]	$4.45x10^{12}$	$4.83x10^{4}$	$2.63x10^{12}$	$6.41x10^{4}$
Herx [31e]	$4.48x10^{12}$	$1.82x10^{4}$	$3.56x10^{12}$	$7.63x10^{4}$
$[Zn(erx)_2(H_2O)_2]$ [31f]	$6.98x10^{12}$	$2.78x10^{4}$	$2.27x10^{12}$	$3.73x10^{4}$
[Zn(erx)(bipy)Cl] [30a]	$5.08x10^{12}$	$5.76x10^{4}$	$2.90x10^{12}$	$4.03x10^{4}$
[Zn(erx)(phen)Cl] [30a]	$5.54x10^{12}$	$1.40x10^{5}$	$4.70x10^{12}$	$3.63x10^{5}$
$[Zn(erx)_2(bipy)]$ [31f]	$6.82x10^{12}$	$3.89x10^{4}$	$6.94x10^{12}$	$3.39x10^{4}$
$[Zn(erx)_2(phen)]$ [31f]	$6.29x10^{12}$	$2.09x10^{4}$	$5.66x10^{12}$	$3.38x10^{4}$
Hsf [31a]	$1.04x10^{13}$	$6.30x10^{4}$	$1.26x10^{13}$	$6.04x10^{4}$
$[Zn(sf)_2(H_2O)_2]$ [31a]	$3.68x10^{13}$	$1.77x10^{5}$	$2.38x10^{13}$	$1.78x10^{5}$
$[Zn(sf)_2(bipy)]$ [31a]	$2.76x10^{13}$	$8.89x10^{4}$	$1.53x10^{13}$	$6.56x10^{4}$
$[Zn(sf)_2(phen)]$ [31a]	$5.19x10^{13}$	$1.99x10^{5}$	$3.34x10^{13}$	$2.20x10^{5}$
$[Zn(sf)_2(bipyam)]$ [31a]	$3.29x10^{13}$	$9.14x10^{4}$	$3.78x10^{13}$	$2.17x10^{4}$
Hlevo [31a]	$9.47x10^{12}$	$3.59x10^{4}$	$8.43x10^{11}$	$1.15x10^{5}$
$[Zn(levo)_2(H_2O)_2]$ [31a]	$3.04x10^{13}$	$1.47x10^{4}$	$2.94x10^{12}$	$1.68x10^{5}$
$[Zn(levo)_2(bipyam)]$ [31a]	$3.98x10^{13}$	$1.62x10^{4}$	$1.68x10^{12}$	$1.93x10^{5}$

Table S9. The SA quenching and binding constants (k_q and K) for the Co(II)-NSAID complexes.

Compound	$\mathbf{k_{q(BSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(BSA)}\ (M^{-1})}$	$\mathbf{k_{q(HSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(HSA)}\ (M^{-1})}$
Hmef [36a]	2.78×10^{13}	1.35×10^{5}	7.13×10^{12}	1.32×10^{5}
$[Co(mef)_2(MeOH)_4]$ [36a]	2.11×10^{14}	2.22×10^{5}	1.96×10^{13}	1.46×10^{5}
$[Co(mef)_2(bipy)(MeOH)_2]$ [36a]	2.86×10^{14}	2.38×10^{5}	1.88×10^{13}	1.34×10^{5}
$[Co(mef)_2(phen)(MeOH)_2]$ [36a]	6.04×10^{13}	3.66×10^{5}	2.29×10^{13}	1.49×10^{5}
$[Co(mef)_2(py)_2(MeOH)_2]$ [36a]	6.32×10^{13}	2.37×10^{5}	1.03×10^{13}	2.43×10^{5}
Hnap [36c]	1.18×10^{12}	5.35×10^{3}	1.24×10^{12}	3.27×10^{4}
$[Co(nap)_2(MeOH)_4]$ [36c]	2.47×10^{12}	1.25×10^{5}	2.42×10^{12}	3.20×10^{4}
$[Co(nap)_2(bipy)(H_2O)_2]$ [36c]	1.75×10^{12}	3.06×10^{4}	6.28×10^{12}	2.19×10^{4}
$[Co(nap)_2(phen)(H_2O)_2]$ [36c]	2.09×10^{12}	1.07×10^{5}	4.23×10^{12}	1.58×10^{4}
$[Co(nap)_2(py)_2(H_2O)_2]$ [36c]	1.21×10^{12}	2.64×10^{4}	1.60×10^{12}	2.69×10^{4}
Htolf [36b]	2.18×10^{13}	1.60×10^{5}	6.10×10^{12}	3.12×10^{5}
$[Co(tolf)_2(MeOH)_4]$ [36b]	2.88×10^{13}	1.11×10^{6}	5.71×10^{12}	4.62×10^{5}
$[Co(tolf)_2(bipy)(MeOH)_2]$ [36b]	8.60×10^{12}	1.39×10^{5}	1.15×10^{12}	3.40×10^{4}
$[Co(tolf)_2(phen)(MeOH)_2]$ [36b]	3.02×10^{13}	6.18×10^{5}	5.27×10^{12}	5.88×10^{5}
$[Co(tolf)_2(bipyam)]$ [36b]	4.30×10^{13}	6.68×10^{5}	5.04×10^{12}	2.20×10^{4}
$[Co(tolf)_2(py)_2(MeOH)_2]$ [36b]	2.74×10^{13}	3.65×10^{5}	3.40×10^{12}	5.74×10^{4}

Table S10. The SA quenching and binding constants (k_q and K) for the Cu(II)-NSAID complexes.

Compound	$\mathbf{k_{q(BSA)}}$ **($M^{-1} s^{-1}$)**	$\mathbf{K_{(BSA)}}$ **(M^{-1})**	$\mathbf{k_{q(HSA)}}$ **($M^{-1} s^{-1}$)**	$\mathbf{K_{(HSA)}}$ **(M^{-1})**
Hnap [38b]	1.18×10^{12}	5.35×10^{3}	1.24×10^{12}	3.27×10^{4}
$[Cu_2(nap)_4(H_2O)_2]$ [38b]	2.34×10^{12}	6.61×10^{4}	4.73×10^{12}	7.83×10^{4}
$[Cu(nap)_2(py)_2(H_2O)]$ [38b]	2.33×10^{12}	2.55×10^{4}	4.56×10^{12}	9.55×10^{3}
$[Cu(nap)_2(bipy)]$ [38b]	2.24×10^{12}	1.20×10^{4}	4.70×10^{12}	3.20×10^{4}
$[Cu(nap)_2(phen)]$ [38b]	2.94×10^{12}	1.90×10^{4}	4.02×10^{12}	7.69×10^{4}
Na dicl [38b]	8.11×10^{12}	3.55×10^{5}	1.81×10^{12}	1.63×10^{5}
$[Cu_2(dicl)_4(H_2O)_2]$ [38b]	1.90×10^{13}	1.72×10^{5}	4.62×10^{12}	1.60×10^{5}
$[Cu(dicl)_2(py)_2]$ [38b]	1.27×10^{13}	5.63×10^{4}	7.62×10^{12}	1.67×10^{5}
$[Cu(dicl)_2(phen)]$ [38b]	1.89×10^{13}	1.62×10^{5}	9.95×10^{12}	1.88×10^{5}
Hmef [38a]	2.78×10^{13}	1.35×10^{5}	7.13×10^{12}	1.32×10^{5}
$[Cu_2(mef)_4(H_2O)_2]$ [38a]	9.86×10^{13}	2.47×10^{5}	1.15×10^{13}	1.69×10^{5}
$[Cu(mef)_2(py)_2(MeOH)_2]$ [38a]	1.31×10^{14}	2.33×10^{5}	1.26×10^{13}	2.21×10^{5}
$[Cu(mef)_2(bipy)]$ [38a]	3.76×10^{13}	1.58×10^{5}	2.44×10^{13}	1.37×10^{5}
$[Cu(mef)_2(phen)]$ [38a]	6.12×10^{13}	2.59×10^{5}	2.08×10^{13}	1.61×10^{5}
$[Cu(mef)_2(bipyam)]$ [38a]	2.88×10^{14}	1.28×10^{6}	3.34×10^{13}	2.52×10^{5}
Hdifl [37b]	1.53×10^{13}	1.93×10^{5}	2.67×10^{12}	1.22×10^{5}
$[Cu_2(difl)_4(DMF)_2]$ [37b]	3.09×10^{13}	4.21×10^{5}	3.07×10^{12}	2.27×10^{5}
$[Cu(difl)_2(py)_2]$ [37b]	6.16×10^{13}	2.42×10^{5}	4.41×10^{12}	2.44×10^{5}
$[Cu(difl)_2(bipy)]$ [37b]	5.95×10^{13}	2.80×10^{5}	4.66×10^{13}	2.68×10^{5}
$[Cu(difl)_2(phen)]$ [37b]	8.87×10^{14}	1.57×10^{5}	2.41×10^{13}	1.59×10^{5}
$[Cu(difl)_2(bipyam)]$ [37b]	1.49×10^{14}	7.98×10^{5}	3.77×10^{13}	2.59×10^{5}

Table S11. The SA quenching and binding constants (k_q and K) for the Htolf and its complexes.

Compound	$\mathbf{k_{q(BSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(BSA)}\ (M^{-1})}$	$\mathbf{k_{q(HSA)}\ (M^{-1}\ s^{-1})}$	$\mathbf{K_{(HSA)}\ (M^{-1})}$
Htolf [35a]	2.18×10^{13}	1.60×10^{5}	0.61×10^{13}	3.12×10^{5}
$[Zn_3(tolf)_6(CH_3OH)_2]$ [35a]	1.87×10^{14}	2.07×10^{5}	1.39×10^{13}	4.12×10^{5}
[Zn(tolf)(phen)Cl] [35a]	9.99×10^{13}	5.70×10^{4}	1.41×10^{13}	4.37×10^{5}
[Zn(tolf)(bipy)Cl] [35a]	1.15×10^{13}	1.81×10^{5}	0.86×10^{13}	1.43×10^{5}
$[Zn(tolf)_2(phen)]$ [35a]	1.00×10^{14}	1.88×10^{5}	4.27×10^{13}	1.36×10^{5}
$[Zn(tolf)_2(bipy)]$ [35a]	3.67×10^{13}	6.20×10^{4}	2.84×10^{13}	1.49×10^{5}

Table S12. Minimum inhibitory concentration (MIC, in $\mu g \cdot mL^{-1}$) of diverse metal-quinolone complexes

Compound	*E. coli*	*P. aeruginosa*	*S. aureus*
Hoxo [37f]	1	16	16
$[Cu(oxo)_2(H_2O)]$ [37f]	64	32	64
$[UO_2(oxo)_2]$ [44a]	64	64	128
$[MoO_2(oxo)_2]$ [44a]	64	64	64
HPPA [44b]	64	64	16
$[VO(PPA)_2(H_2O)]$ [44b]	64	64	16
$[Mn(PPA)_2(H_2O)_2]$ [44b]	64	64	16
$[Fe(PPA)_3]$ [44b]	64	64	32
$[Co(PPA)_2(H_2O)_2]$ [44b]	64	64	32
$[Ni(PPA)_2(H_2O)_2]$ [44b]	64	32	32
$[Cu(PPA)_2(H_2O)]$ [44c]	8	8	16
$[Zn(PPA)_2(H_2O)_2]$ [44b]	32	32	32
$[MoO_2(PPA)_2]$ [44b]	64	64	16
$[Cd(PPA)_2(H_2O)_2]$ [44b]	64	64	16
$[UO_2(PPA)_2]$ [44b]	8	8	8
Hpr-norf [44d]	4	4	16
$[VO(pr\text{-}norf)_2(H_2O)]$ [44d]	4	4	16
$[Mn(pr\text{-}norf)_2(H_2O)_2]$ [44d]	8	4	16
$[Fe(pr\text{-}norf)_3]$ [44d]	8	8	32
$[Co(pr\text{-}norf)_2(H_2O)_2]$ [44d]	8	16	16
$[Ni(pr\text{-}norf)_2(H_2O)_2]$ [44d]	8	8	16
$[Cu(pr–norf)_2(H_2O)]$ [44c]	0.5	8	8
$[Zn(pr\text{-}norf)_2(H_2O)_2]$ [44d]	16	8	32
$[MoO_2(pr\text{-}norf)_2]$ [44d]	4	4	16
$[Cd(pr\text{-}norf)_2(H_2O)_2]$ [44d]	8	8	16
$[UO_2(pr\text{-}norf)_2]$ [44d]	8	16	4
Herx [27e]	1.0	1.0	8.0
$[VO(erx)_2(H_2O)]$ [44e]	4.0	4.0	8.0
$[Mn(erx)_2(H_2O)_2]$ [44f]	1.0	1.0	8.0
$[Fe(erx)_3]$ [44f]	0.25	0.25	2.0

$[Co(erx)_2(H_2O)_2]$ [44f]	1.0	1.0	2.0
$[Ni(erx)_2(H_2O)_2]$ [44f]	1.0	1.0	8.0
$[Cu(erx)_2(H_2O)]$ [27e]	0.125	0.125	4.0
$[Zn(erx)_2(H_2O)_2]$ [44f]	1.0	1.0	2.0
$[Cd(erx)_2(H_2O)_2]$ [44f]	1.0	1.0	8.0
$[UO_2(erx)_2]$ [44f]	1.0	1.0	8.0
$[MoO_2(erx)_2]$ [44g]	1.0	1.0	4.0
Hsf [26a]	8	0.5	0.5
$[VO(sf)_2(H_2O)]$ [44h]	64	16	64
$[Mn(sf)_2(H_2O)_2]$ [44h]	128	128	128
$[Fe(sf)_3]$ [44h]	64	32	64
$[Co(sf)_2(H_2O)_2]$ [44i]	4	1	2
$[Ni(sf)_2(H_2O)_2]$ [25c]	16	128	16
$[Cu(sf)_2]$ [26a]	2	0.25	1
$[UO_2(sf)_2]$ [44h]	128	32	128
$[MoO_2(sf)_2]$ [44g]	4	1	2

Table S13. Minimum inhibitory concentration (MIC, in $\mu g \cdot mL^{-1}$) of diverse copper(II)-quinolone complexes.

Compound	*E. coli*	*P. aeruginosa*	*S. aureus*
Hoxo [27f]	1.0	16	16
$[Cu(oxo)_2(H_2O)]$ [27f]	64	32	64
[Cu(oxo)(bipy)Cl] [27f]	64	32	64
[Cu(oxo)(phen)Cl] [27f]	64	64	32
[Cu(oxo)(bipyam)Cl] [27f]	64	64	64
HPPA [44c]	64.0	64.0	16.0
$[Cu(PPA)_2(H_2O)]$ [44c]	8	8	16
[Cu(PPA)(bipy)Cl] [44c]	8	16	8
[Cu(PPA)(phen)Cl] [44c]	4	4	8
[Cu(PPA)(bipyam)Cl] [44c]	16	16	32
Herx [27e]	1.0	1.0	8.0
$[Cu(erx)_2(H_2O)]$ [27e]	0.125	0.125	4
$[Cu(erx)(bipy)(H_2O)]Cl$ [27e]	1	0.5	4
[Cu(erx)(phen)Cl] [27e]	2	1	4
Hpr-norf [27a]	4.0	4.0	16.0
$[Cu(pr–norf)_2(H_2O)]$ [44c]	0.5	8	8
[Cu(pr–norf)(bipy)Cl] [27a]	0.25	8	8
[Cu(pr–norf)(phen)Cl] [45a]	2	0.25	16
[Cu(pr–norf)(bipyam)Cl] [44c]	4	4	8
Hsf [26a]	8	0.25	0.5
$[Cu(sf)_2]$ [26a]	2	0.25	1
[Cu(sf)(bipy)Cl] [45b]	2	0.5	2
[Cu(sf)(phen)Cl] [45b]	2	0.5	2
[Cu(sf)(bipyam)Cl] [45b]	2	1	4

Table S14. Interaction % with DPPH (RA%), superoxide radical scavenging activity (ABTS%) and competition % with DMSO for hydroxyl radical (·OH%) of 0.1 mM solution and *in vitro* inhibition of soybean lipoxygenase (LOX) (IC_{50}, μM)of the quinolones and their Ni(II) complexes.

Compound	**(RA%)**	**ABTS%**	**·OH%**	**LOX (IC_{50}, μM)**
Hoxo [25f]	18.17	23.83	39.56	62.8
$[Ni(oxo)_2(H_2O)_2]$ [25f]	41.42	32.86	57.68	32.7
$[Ni(oxo)_2(py)_2]$ [25f]	36.83	16.89	41.36	42.4
$[Ni(oxo)_2(4bzpy)_2]$ [25f]	30.66	22.26	37.39	48.7
$[Ni(oxo)_2(bipy)]$ [25f]	30.43	27.45	39.79	46.1
$[Ni(oxo)_2(phen)]$ [25f]	23.15	22.37	38.39	39.8
$[Ni(oxo)_2(bipyam)]$ [25f]	34.61	24.14	42.27	52.9
Hflmq [25f]	13.04	15.48	21.58	40.3
$[Ni(flmq)_2(H_2O)_2]$ [25f]	28.70	30.63	34.37	26.2
$[Ni(flmq)_2(py)_2]$ [25f]	20.38	27.12	21.03	36.7
$[Ni(flmq)_2(4bzpy)_2]$ [25f]	19.22	27.48	20.33	27.8
$[Ni(flmq)_2(bipy)]$ [25f]	12.74	12.69	31.24	31.2
$[Ni(flmq)_2(phen)]$ [25f]	22.16	29.58	25.84	32.9
$[Ni(flmq)_2(bipyam)]$ [25f]	22.43	26.39	19.32	29.6
Herx [25f]	14.06	24.79	32.41	60.3
$[Ni(erx)_2(H_2O)_2]$ [25f]	26.20	34.65	46.34	30.3
$[Ni(erx)_2(py)_2]$ [25f]	16.62	28.58	34.76	50.3
$[Ni(erx)_2(4bzpy)_2]$ [25f]	19.10	22.31	27.06	53.9
$[Ni(erx)_2(bipy)]$ [25f]	23.83	26.54	37.23	48.9
$[Ni(erx)_2(phen)]$ [25f]	19.50	24.72	31.12	49.2
$[Ni(erx)_2(bipyam)]$ [25f]	21.70	29.43	34.68	51.8
Hsf [25f]	16.87	24.43	29.42	52.4
$[Ni(sf)_2(H_2O)_2]$ [25f]	24.88	29.09	43.22	29.3
$[Ni(sf)_2(py)_2]$ [25f]	21.39	28.76	31.84	40.2
$[Ni(sf)_2(4bzpy)_2]$ [25f]	11.18	23.47	27.61	55.1
$[Ni(sf)_2(bipy)]$ [25f]	20.01	28.30	36.62	38.6
$[Ni(sf)_2(phen)]$ [25f]	19.95	21.46	33.00	43.0
$[Ni(sf)_2(bipyam)]$ [25f]	16.87	22.00	26.57	35.2
NDGA [25f]	82.60	--	--	--
BHT [25f]	60.00	--	--	--
Trolox [25f]	--	91.80	82.80	--
Caffeic acid [25f]	--	--	--	600.0

Table S15. Interaction % with DPPH (RA%), superoxide radical scavenging activity (ABTS%) and competition % with DMSO for hydroxyl radical (·OH%) of 0.1 mM solution of the NSAIDs and their Co(II) complexes.

Compound	**RA%**	**ABTS%**	**·OH%**
Hmef [36a]	11.7	66.3	92.5
$[Co(mef)_2(MeOH)_4]$ [36a]	30.1	78.3	95.7
$[Co(mef)_2(py)_2(MeOH)_2]$ [36a]	29.5	97.0	96.7
$[Co(mef)_2(bipy)(MeOH)_2]$ [36a]	17.9	92.4	96.4
$[Co(mef)_2(phen)(MeOH)_2]$ [36a]	36.8	90.4	89.3
Hnap [36c]	8.43	87.51	89.55
$[Co(nap)_2(MeOH)_4]$ [36c]	20.37	82.46	96.75
$[Co(nap)_2(py)_2(H_2O)_2]$ [36c]	18.90	90.22	84.98
$[Co(nap)_2(bipy)(H_2O)_2]$ [36c]	26.98	84.54	90.21
$[Co(nap)_2(phen)(H_2O)_2]$ [36c]	42.42	87.32	92.46
NDGA [36a]	82.6	--	--
BHT [36a]	60	--	--
Trolox [36a]	--	91.8	88.2

Table S16. Interaction % with DPPH (RA%), superoxide radical scavenging activity (ABTS%), competition % with DMSO for hydroxyl radical (·OH%) of 0.1 mM solution of the NSAIDs and their Cu(II) complexes. *In vitro* inhibition of soybean lipoxygenase (LOX) (IC_{50}, μM).

Compound	**RA%**	**ABTS%**	**·OH%**	**LOX IC_{50} (μM)**
Hmef [38a]	11.7	66.3	92.5	48.5
$[Cu_2(mef)_4(H_2O)_2]$ [38a]	54.1	75.4	67.6	4.8
$[Cu(mef)_2(py)_2(MeOH)_2]$ [38a]	21.5	98.2	75.3	50
$[Cu(mef)_2(bipy)]$ [38a]	7.9	90.3	74.6	40
$[Cu(mef)_2(phen)]$ [38a]	7.9	89.4	99.7	67.5
$[Cu(mef)_2(bipyam)]$ [38a]	18.5	80.0	77.4	54.5
Hnap [36c]	8.43	87.51	89.55	
$[Cu(nap)_2(H_2O)]_2$ [36c]	20.16	77.74	72.84	
$[Cu(nap)_2(py)_2(H_2O)]$ [36c]	18.66	92.12	93.40	
$[Cu(nap)_2(bipy)]\cdot H_2O$ [36c]	19.48	76.44	80.11	
$[Cu(nap)_2(phen)]\cdot H_2O$ [36c]	18.76	82.39	93.26	
NDGA [38a]	82.6			
BHT [38a]	60			
Trolox [38a]		91.8	88.2	
Caffeic acid [38a]				600