

Supplementary material.

Bathophenanthroline copper complexes as candidates to antitumor drugs. Synthesis, characterization, DNA interaction and cytotoxicity studies of a series of copper(II)-L-dipeptide-bathophenanthroline complexes.

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Figure S1. Space fill representation of the optimized structure of compound 3.

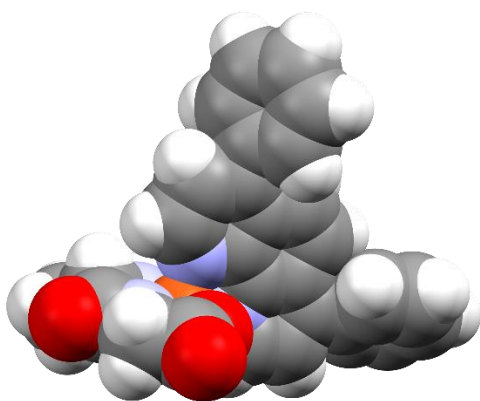


Table S1. DNA binding constants (K_b) determined by the Benesi-Hildebrand method. For comparison previously determined values of related complexes are also included.

Complex	Code	K_b ($\times 10^3$ M ⁻¹)
[Cu(phen)] ²⁺	-	5.4 [1]
[Cu(neo)] ²⁺	-	3.6 [2]
[Cu(tmp)] ²⁺	-	2.2 [3]
[Cu(batho)] ²⁺	C0	1.3
[Cu(gly-val)(batho)]	C1	2.0
[Cu(gly-phe)(batho)]	C3	0.9
[Cu(ala-gly)(batho)]	C4	2.3
[Cu(ala-phe)(batho)]	C6	0.3
[Cu(phe-ala)(batho)]	C7	1.0

[Cu(phe-val)(batho)]	C7	0.8
[Cu(phe-phe)(batho)]	C7	1.0

Table S2. Aproximated DNA slope of the variation of the viscosity induced by the binding of the complexes

Complex	Slope
[CuCl ₂ (phen)]	0.24
[Cu(ala-phe)(phen)]	0.21
[Cu(ala-gly)(phen)]	0.24
phen	0.07
[CuCl ₂ (neo)]	0.13
[Cu(ala-phe)(neo)]	0.12
[Cu(ala-gly)(neo)]	0.14
neo	0.12
[CuCl ₂ (tmp)]	0.07
[Cu(ala-phe)(tmp)]	-0.03
[Cu(ala-gly)(tmp)]	0.10
tmp	0.12
[CuCl ₂ (batho)]	-0.28
[Cu(ala-phe)(batho)]	-0.29
[Cu(ala-gly)(batho)]	-0.24
batho	-0.36

Table S3. Selectivity index of the compounds (SI, IC₅₀ on non tumor cells /IC₅₀ on tumor cells of related origin)

Compound	SI (MCF-10/MDA-MB-231-)	SI (MCF-10/MCF-7)	SI (MRC-5/A549)
[Cu(gly-val)(batho)]	12.07	12.38	0.50
[Cu(gly-phe)(batho)]	4.55	3.77	0.97
[Cu(ala-gly)(batho)]	1.26	4.98	0.07
[Cu(ala-ala)(batho)]	7.66	2.48	0.68
[Cu(ala-phe)(batho)]	3.98	2.59	0.47
[Cu(phe-ala)(batho)]	2.25	3.36	0.76
[Cu(phe-val)(batho)]	5.77	2.44	0.24

[Cu(phe-phe)(batho)]	4.04	1.28	0.62
[CuCl ₂ (batho)]	5.85	1.00	0.98
Cisplatin	1.92	2.68	2.02

References

1. Iglesias, S., et al., *Synthesis, structural characterization and cytotoxic activity of ternary copper (II)-dipeptide-phenanthroline complexes. A step towards the development of new copper compounds for the treatment of cancer*. Journal of Inorganic Biochemistry, 2014. **139**: p. 117-123.
2. Alvarez, N., et al., *Synthesis and structural characterization of a series of ternary copper (II)-L-dipeptide-neocuproine complexes. Study of their cytotoxicity against cancer cells including MDA-MB-231, triple negative breast cancer cells*. Journal of Inorganic Biochemistry, 2020. **203**: p. 110930.
3. Alvarez, N., et al., *Tetramethyl-phenanthroline copper complexes in the development of drugs to treat cancer: synthesis, characterization and cytotoxicity studies of a series of copper(II)-L-dipeptide-3,4,7,8-tetramethyl-phenanthroline complexes*. JBIC Journal of Biological Inorganic Chemistry, 2022.