

Copper complexes with analogues of natural compounds exhibiting potential antitumor activity

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Isatin is an oxindole found in mammal tissues and widely studied; it has some biological properties including antiproliferative and antitumor activity. A copper(II) complex with a Schiff base ligand derived from isatin, [Cu(*isaepy*)], has been synthesized in our laboratory, and showed cytotoxicity against U937 promonocytic cells and SH-SY5Y neuroblastoma cells. It also has an important ability to bind to DNA, causing significant oxidative damage and inducing apoptosis^{1,2}. *Dicathais orbita* is an Australian marine gastropod that produces several brominated oxindoles, like 6-bromoisatin, that is capable of inducing apoptosis in the H2T9 colon cancer cells³. Furthermore, halogenated isatins demonstrated an increased citotoxic activity against U937 promonocytic cells compared to unsubstituted isatin⁴. Based on this information, our study aimed on the synthesis of brominated analogues of [Cu(*isaepy*)] in order to verify a possible increasing in its anticancer activity. The syntheses of analogous complexes were carried out in ethanol, reacting 5-bromoisatin (5-Brisa) or 5,7-bromoisatin (5,7-Brisa) with 2,2-aminoethylpyridine (epy) under acid catalysis. Copper perchlorate was then added to metallate the prepared imine ligand. Complex structures were confirmed by elemental analysis, and spectroscopic data from infrared, UV/Vis and EPR. MTT assay was performed using uterine sarcoma cell lines MES-SA and resistant MES-SA Dx5, after 24h incubation at 37°C, with the aim of comparing the reactivity of such new complexes. Results showed that the brominated complexes show similar cytotoxic activity to that of [Cu(*isaepy*)], the most active compound in a series of oxindolimine complexes studied in our lab.

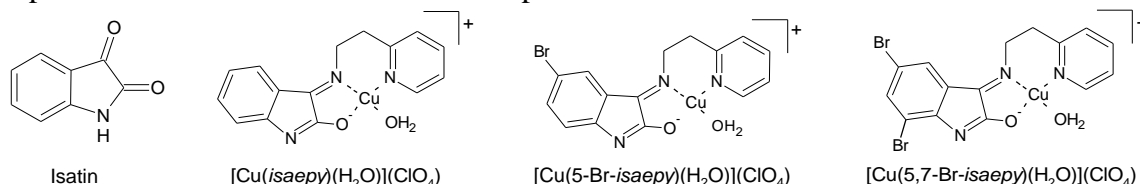


Fig. 1- Structure of isatin and studied complexes.

	<u>MES-SA</u>	<u>MES-SA/Dx5</u>
[Cu(<i>isaepy</i>)]	19,7 ± 1,8	12,4 ± 0,4
[Cu(5-Br- <i>isaepy</i>)]	33,3 ± 7,3	21,3 ± 3,5
[Cu(5,7-Br- <i>isaepy</i>)]	21,4 ± 2,7	11,5 ± 0,6

Table - IC₅₀ values (μM) for the tested compounds, compared to [Cu(*isaepy*)].

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