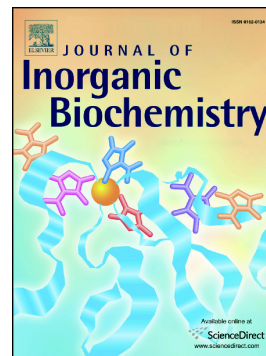


Accepted Manuscript

Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets

Xiangchao Shi, Hongbao Fang, Yan Guo, Hao Yuan, Zijian Guo, Xiaoyong Wang



PII: S0162-0134(18)30461-6
DOI: doi:[10.1016/j.jinorgbio.2018.10.003](https://doi.org/10.1016/j.jinorgbio.2018.10.003)
Reference: JIB 10577

To appear in: *Journal of Inorganic Biochemistry*

Received date: 3 August 2018
Revised date: 9 October 2018
Accepted date: 12 October 2018

Please cite this article as: Xiangchao Shi, Hongbao Fang, Yan Guo, Hao Yuan, Zijian Guo, Xiaoyong Wang , Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets. Jib (2018), doi:[10.1016/j.jinorgbio.2018.10.003](https://doi.org/10.1016/j.jinorgbio.2018.10.003)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Anticancer copper complex with nucleus, mitochondrion and cyclooxygenase-2 as multiple targets

Xiangchao Shi,^a Hongbao Fang,^a Yan Guo,^a Hao Yuan,^a Zijian Guo*^a and Xiaoyong Wang*^b

^a State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210023, P. R. China. E-mail: zguo@nju.edu.cn; Fax: +86 25 83314502

^b State Key Laboratory of Pharmaceutical Biotechnology, School of Life Sciences, Nanjing University, Nanjing 210023, P. R. China. E-mail: boxwxy@nju.edu.cn; Fax: +86 25 83314502

Abstract: Copper complexes are hopeful anticancer drugs due to their multifacet biological properties and high biocompatibility. Inflammatory environment plays an important role in tumor progression and affects the body response to chemotherapeutic agents. A copper(II) complex CuLA with a phenanthroline derivative N-(1,10-phenanthroline-5-yl)-nonanamide (L) and two aspirin anions (A) as the ligands was synthesized. CuLA effectively induces mitochondrial dysfunction and promotes early-apoptosis in SKOV-3 cells; moreover, it suppresses the expression of cyclooxygenase-2, a key enzyme involved in inflammatory response, in lipopolysaccharide stimulated RAW 264.7 cells. By contrast, the analogue complex CuL without aspirin ligand shows similar influences on cellular redox homeostasis and cell cycle progression but relatively low cytotoxic activity due to its mild effect on mitochondrial function; more importantly, it lacks inhibition to cyclooxygenase-2. The results demonstrate that CuLA inhibits cancer cells through dual pathways involving DNA damage and mitochondrial dysfunction. The introduction of aspirin not only enhances the antitumor efficacy but also reduces the inflammatory threat. Copper complexes with both antitumor and anti-inflammatory activities may

Download English Version:

<https://daneshyari.com/en/article/12121868>

Download Persian Version:

<https://daneshyari.com/article/12121868>

[Daneshyari.com](https://daneshyari.com)