Journal of Inorganic Biochemistry 154 (2016) 67–77

Contents lists available at ScienceDirect

Journal of Inorganic Biochemistry

journal homepage: www.elsevier.com/locate/jinorgbio

Low-dimensional compounds containing bioactive ligands. Part VI: Synthesis, structures, *in vitro* DNA binding, antimicrobial and anticancer properties of first row transition metal complexes with 5-chloro-quinolin-8-ol

Ivan Potočňák [a,*], Peter Vranec [a], Veronika Farkasová [a], Danica Sabolová [b], Michaela Vataščinová [b], Júlia Kudláčová [b], Ivana D. Radojević [c], Ljiljana R. Čomić [c], Bojana Simovic Markovic [d], Vladislav Volarevic [d], Nebojsa Arsenijevic [d], Srećko R. Trifunović [e]

[a] Department of Inorganic Chemistry, Institute of Chemistry, P. J. Šafárik University, Moyzesova 11, SK-04154 Košice, Slovak Republic
[b] Department of Biochemistry, Institute of Chemistry, P. J. Šafárik University, Moyzesova 11, SK-04154 Košice, Slovak Republic
[c] Department of Biology and Ecology, Faculty of Science, University of Kragujevac, Radoja Domanovića 12, 34000 Kragujevac, Serbia
[d] Centre for Molecular Medicine and Stem Cell Research, Faculty of Medical Sciences, University of Kragujevac, 69 Svetozara Markovica, 34000 Kragujevac, Serbia
[e] Department of Chemistry, Faculty of Science, University of Kragujevac, Radoja Domanovića 12, 34000 Kragujevac, Serbia

ARTICLE INFO

Article history:
Received 13 May 2015
Received in revised form 12 October 2015
Accepted 28 October 2015
Available online 31 October 2015

Keywords:
5-Chloro-quinolin-8-ol complexes
Cytotoxicity
Antimicrobial activity
DNA-binding properties
Topoisomerase I inhibition

ABSTRACT

A series of new 3d metal complexes with 5-chloro-quinolin-8-ol (ClQ), $[Mn(ClQ)_2]$ (**1**), $[Fe(ClQ)_3]$ (**2**), $[Co(ClQ)_2(H_2O)_2]$ (**3**), $[Ni(ClQ)_2(H_2O)_2]$ (**4**), $[Cu(ClQ)_2]$ (**5**), $[Zn(ClQ)_2(H_2O)_2]$ (**6**), $[Mn(ClQ)_3]\cdot DMF$ (**7**) and $[Co(ClQ)_3]\cdot DMF\cdot(EtOH)_{0.35}$ (**8**) (DMF = *N*,*N*-dimethylformamide), has been synthesized and characterized by elemental analysis, IR spectroscopy and TG–DTA thermal analysis. X-ray structure analysis of **7** and **8** revealed that these molecular complexes contain three chelate ClQ molecules coordinated to the central atoms in a deformed octahedral geometry and free space between the complex units is filled by solvated DMF and ethanol molecules. Antimicrobial activity of **1**–**6** was tested by determining the minimum inhibitory concentration and minimum microbicidal concentration against 12 strains of bacteria and 5 strains of fungi. The intensity of antimicrobial action varies depending on the group of microorganism and can be sorted: **1** > ClQ > **6** > **3**/**4** > **2** > **5**. Complexes **1**–**6** exhibit high cytotoxic activity against MDA-MB, HCT-116 and A549 cancer cell lines. Among them, complex **2** is significantly more cytotoxic against MDA-MB cells than cisplatin at all tested concentrations and is not cytotoxic against control mesenchymal stem cells indicating that this complex seems to be a good candidate for future pharmacological evaluation. Interaction of **1**–**6** with DNA was investigated using UV–VIS spectroscopy, fluorescence spectroscopy and agarose gel electrophoresis. The binding studies indicate that **1**–**6** can interact with CT-DNA through intercalation; complex **2** has the highest binding affinity. Moreover, complexes **1**–**6** inhibit the catalytic activity of topoisomerase I.

1. Introduction

Worldwide efforts to overcome limitations of recent metal-based chemotherapy by preparing new coordination compounds as anticancer agents bring together many scientists all over the world [1]. The success of cisplatin and its analogs in the treatment of several cancer cell lines influenced the development of inorganic metal coordination chemistry over the last 40 years. Today cisplatin is considered as one of the most successful drug; however its applications are limited due to its significant side effects and a resistance of human body to this drug [2].

Several strategies have been used to increase tumor cells selectivity and thus decrease toxic side effects of platinum drugs, including the substitution of ligands present at platinum by other biologically active ligands with adequate chelating properties and favorable toxicity profiles. The approach used by our research group is based on coordination of quinolin-8-ol (8-HQ) halogen derivatives to metal ions with the aim to increase the cytotoxicity of prepared complexes in comparison to biological activity of ligands themselves.

A perfect example of 8-HQ halogen derivatives is 5-chloro-7-iodo-quinolin-8-ol (clioquinol, CQ), a chelator of copper, zinc and iron, which was used as an antimicrobial agent [3]. Recently, CQ has been widely investigated as it exhibit activity against Alzheimer's and Parkinson's diseases [4–6]. Its biological effects are most likely ascribed to the complexation of specific metal ions, such as Cu(II) and Zn(II),

* Corresponding author.
E-mail address: ivan.potocnak@upjs.sk (I. Potočňák).

http://dx.doi.org/10.1016/j.jinorgbio.2015.10.015
0162-0134/