Vol. 43 - No. 1 Special Edition 2021

Biologia Serbica

Department of Biology and Ecology,
Faculty of Sciences, University of Novi Sad, Serbia

BELBI 2021

Book of Abstracts
Belgrade BioInformatics Conference 2021
21-25 June 2021, Vinča, Serbia

http://ojs.pmf.uns.ac.rs/index.php/dbe_serbica/index

Biologia Serbica

JUNE 2021
Vol. 43 - No. 1 Special Edition

Biologia Serbica is formerly Review of Research, Faculty of Sciences, Biology Series (1971-2004), published by Department of Biology and Ecology, Faculty of Sciences, University of Novi Sad, Serbia

Aim and Scope

Biologia Serbica (BS) is an international scientific, peer-reviewed, open access journal that publishes original research articles, review articles, and short communications in all areas of biology.

Publisher

Department of Biology and Ecology
Faculty of Sciences
University of Novi Sad
Trg Dositeja Obradovića 2
21000 Novi Sad, Serbia
: +381 21 485 26 59
: +381 21 450 620
www.dbe.uns.ac.rs

Biologia Serbica is published biannually.

Printed by

"Sajnos"
Momčila Tapavice 2,
21000 Novi Sad
+381/21/499-461, +381/21/499-088
sajnosns@gmail.com

Date od publication: June 2018.

Subscription rates

Instructions available at
http://ojs.pmf.uns.ac.rs/index.php/dbe_serbica/index

Inhibitor potential of some Au(III) complexes against SARS-CoV-2 Spike Glycoprotein: A Molecular Docking Study

Žiko Milanović[1*], Ana Kesić[1], Dejan Milenković[1], Edina Avdović[1] and Zoran Marković[1]

[1]*University of Kragujevac, Institute for Information Technologies, Jovana Cvijića bb, 34000 Kragujevac, Serbia*

Abstract

The pharmacologic properties of gold compounds have been known since the end of the 19th century. In the last decade, gold complexes have received increased attention due to the variety of their applications. Square planar Au(III) complexes are suitable candidates for biological investigation because of useful substances with a good stability profile. Some Au(III) complex could be significantly stabilized, even at neutral pH, with the appropriate choice of the inert ligands, preserving its peculiar biological properties. In this paper, the molecular interactions between active binding sites of SARS-CoV-2 Spike Glycoprotein and analyzed compounds, Au(III) complexes ([Au(terpy)Cl]2+ (C1) and [Au(bipy)Cl2]+ (C2),), hydroxychloroquine and chloroquine, were investigated by molecular docking simulations. The crystal structure of investigated receptor (PDB ID: 6VSB) was extracted from RCSB Protein Data Bank in PDB format. The binding affinity of investigated compounds was examined by the AutoDock 4.2 software. AutoDockTools was used to calculate the Kollman partial charges and addition polar hydrogens. The flexibility of the ligands was considered, while the protein kept on as the rigid structure in the ADT. The Lamarckian Genetic Algorithm (LGA) method was used for protein-ligand flexible docking. The parameters for the LGA method were determined as follows: a maximum number of energy evaluations is 250,000, a maximum number of generations is 27,000, and mutation and crossover rates are 0.02 and 0.8, respectively. The pockets and binding sites of the target receptor were determined by the AutoGridFR program. The binding energies of the docked compounds of C1 and C2 against SARS-CoV-2 Spike Glycoprotein were found to be in the range between -28.5 and -23.5 kJ/mol, as opposed to hydroxychloroquine and chloroquine which are -34.5 and -35.8 kJ/mol, respectively. The obtained results revealed that C1 and C2 bind at the same binding pockets to SARS-CoV-2 Spike Glycoprotein, as well as hydroxychloroquine and chloroquine, by weak non-covalent interactions. The most prominent interactions are hydrogen bonds, alkyl-π, and π-π interactions. The preliminary results suggest that Au(III) complexes showed good binding affinity against SARS-CoV-2 Spike Glycoprotein, as evident from the free binding energy (ΔGbind in kJ/mol) and that might exhibit inhibitory activity against SARS-CoV-2 Spike Glycoprotein.

Keywords:

Au(III) complex, terpyridine, bipyridine, molecular docking, SARS-CoV-2 Spike Glycoprotein

Acknowledgments:

Authors acknowledge the Ministry of Education, Science and Technological Development of the Republic of Serbia for the support through Contracts No. 451-03-9/2021-14/200378.

*Corresponding author, e-mail: ziko.milanovic@uni.kg.ac.rs

CIP – Каталогизација у публикацији
Библиотека Матице српске, Нови Сад 57
BIOLOGIA Serbica / editor-in chief Milica Matavulj. –
Vol. 34, no. ½ (dec. 2012) - . – Novi Sad : Faculty of Sciences, Department of Biology and Ecology, 2012-. –
Ilustr. ; 28 cm
Dva puta godišnje. – Je nastavak: Зборник радова Природно-математичког факултета. Серија за биологију = ISSN 0352 – 1788
ISSN 2334 – 6590 = Biologia Serbica
COBISS.SR – ID 275725831

ISSN 2334-6590

2021
Vol. 43 - No. 1 Special Edition

Biologia Serbica

ISSN 2334-6590

Inhibitor potential of some Au(III) complexes against SARS-CoV-2 Spike Glycoprotein: A Molecular Docking Study

Žiko Milanović, Ana Kesić, Dejan Milenković, Edina Avdović and Zoran Marković
University of Kragujevac, Institute for Information Technologies, Jovana Cvijića bb, 34000 Kragujevac, Serbia

INTRODUCTION

The pharmacologic properties of gold compounds have been known since the end of the 19th century. In the last decade, gold complexes have received increased attention due to the variety of their applications. Square planar Au(III) complexes are suitable candidates for biological investigation because of useful substances with a good stability profile. Some Au(III) complex could be significantly stabilized, even at neutral pH, with the appropriate choice of the inert ligands, preserving its peculiar biological properties.

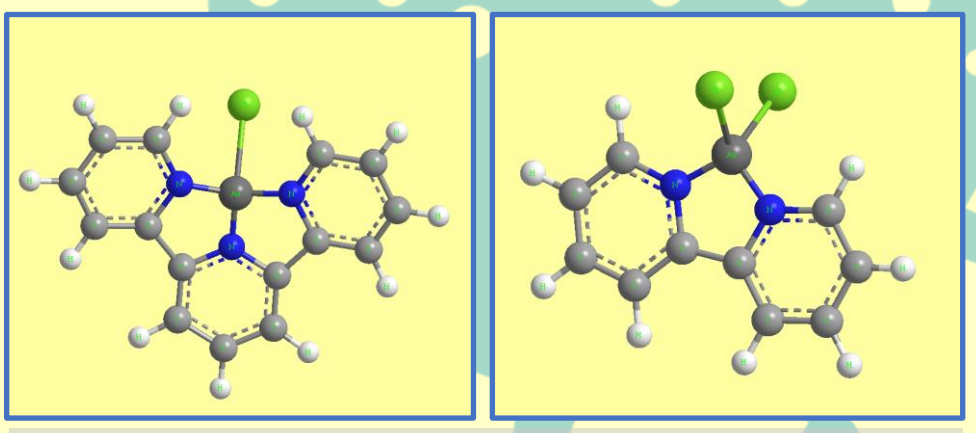
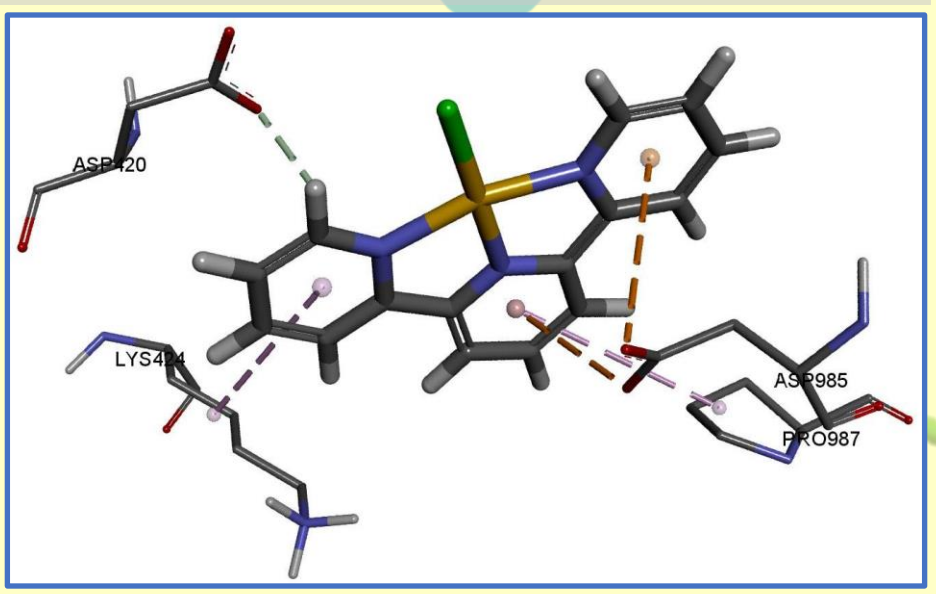


Figure 1. The structure of studied gold(III) complexes ($[Au(terpy)Cl]^{2+}$, **C1** (left) and $[Au(bipy)Cl_2]^{+}$,**C2** (right)



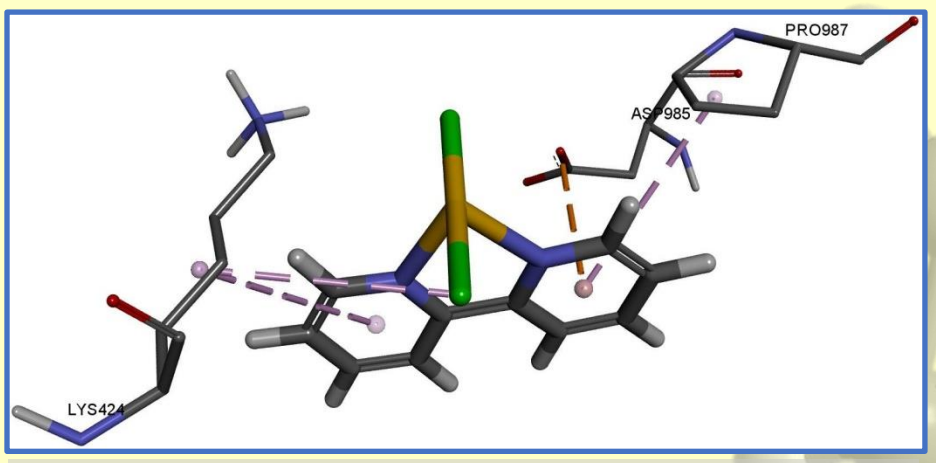


Figure 2. 3D representation of noncovalent interactions between protein and transition metal complexes

Acknowledgments: Authors acknowledge the Ministry of Education, Science and Technological Development of the Republic of Serbia for the support through Contracts No. 451-03-68/2021-14/200378.

METHODOLOGY

In this paper, the molecular interactions between active binding sites of SARS-CoV-2 Spike Glycoprotein and analyzed compounds, Au(III) complexes ($[Au(terpy)Cl]^{2+}$ (**C1**) and $[Au(bipy)Cl_2]^{+}$ (**C2**),), hydroxychloroquine and chloroquine, were investigated by molecular docking simulations. The crystal structure of investigated receptor (PDB ID: 6VSB) was extracted from RCSB Protein Data Bank in PDB format. The binding affinity of investigated compounds was examined by the AutoDock 4.2 software. AutoDockTools was used to calculate the Kollman partial charges and addition polar hydrogens. The flexibility of the ligands was considered, while the protein kept on as the rigid structure in the ADT. The Lamarckian Genetic Algorithm (LGA) method was used for protein-ligand flexible docking. The parameters for the LGA method were determined as follows: a maximum number of energy evaluations is 250,000, a maximum number of generations is 27,000, and mutation and crossover rates are 0.02 and 0.8, respectively. The pockets and binding sites of the target receptor were determined by the AutoGridFR program.

Table 1. Thermodynamic data obtained by docking simulation of tested compounds with SARS-CoV-2 M^{pro}

Compounds:	ΔG_{bind} (kcal mol^{-1})	K_i (uM)
C1	-6.81	10.21
C2	-5.75	60.70
Hydroxychloroquine	-8.24	0.91
Chloroquine	-8.55	0.54

RESULTS

The binding energies of the docked compounds of **C1** and **C2** against SARS-CoV-2 Spike Glycoprotein were found to be in the range between -6.81 and -5.75 kcal mol^{-1}, as opposed to hydroxychloroquine and chloroquine which are -8.24 and -8.55 kcal mol^{-1}, respectively. The obtained results revealed that **C1** and **C2** bind at the same binding pockets to SARS-CoV-2 Spike Glycoprotein, as well as hydroxychloroquine and chloroquine, by weak non-covalent interactions. The most prominent interactions are hydrogen bonds, alkyl-π, and π-π interactions.

CONCLUSION

The preliminary results suggest that Au(III) complexes showed good binding affinity against SARS-CoV-2 Spike Glycoprotein.