Inorganic Chemistry Communications 143 (2022) 109779

Contents lists available at ScienceDirect

Inorganic Chemistry Communications

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

Short communication

Dual inhibition of *S. aureus TyrRS* and *S. aureus gyrase* by two 4-amino-4′-acetyldiphenyl sulfide-based Schiff bases: Structural features, DFT study, *Hirshfeld* surface analysis and molecular docking

Soumia Kadri [a], Amani Direm [b,*], Hamza Athmani [b], Brahim El Bali [c], Cemal Parlak [d], Rabihe Hebbachi [a]

[a] *Environmental and Structural Molecular Chemistry Research Unit, Faculty of Exact Sciences, Department of Chemistry, University of Mentouri Brothers, Constantine 1, Constantine 25.000, Algeria*
[b] *Laboratory of Structures, Properties and Interatomic Interactions LASPI²A, Department of Matter Sciences, Faculty of Sciences and Technology, Abbes Laghrour University, Khenchela 40.000, Algeria*
[c] *Independent Scientist, Marrakech, Morocco*
[d] *Department of Physics, Science Faculty, Ege University, Izmir 35100, Turkey*

ARTICLE INFO

Keywords:
Schiff bases
Staphylococcus *aureus*
Antimicrobial resistance
Dual inhibition
DFT
Hirshfeld surface analysis
Molecular docking

ABSTRACT

Two 4-amino-4′-acetyldiphenyl sulfide-based Schiff bases, namely 1-[4-({4-[(E)-(2-hydroxynaphthalen-1-yl) methylideneamino]phenyl}sulfanyl)-phenyl]ethanone (**I**) and (E)-1-[4-({4-[(4-methoxybenzylidene)amino] phenyl}-sulfanyl)phenyl]ethan-1-one (**II**) were structurally studied. They crystallize respectively in the monoclinic *Cc* and the triclinic *P*1 space groups, with the respective cell parameters: [10.695(3) Å, 44.458(14) Å, 4.4437(11) Å, 99.004(9)°] and [5.7708(2) Å, 8.0867(3) Å, 19.6929(8) Å, 81.844(2)°, 86.664(3)°, 85.662(3)°]. The asymmetric units of (**I**) and (**II**) are composed of one molecule and two crystallographically independent molecules, respectively. Their molecular structures were optimized by the density functional theory and correlated correspondingly to the crystal structures. Moreover, the IR vibration modes were assigned to the calculated wavenumbers, the *Mulliken* atomic charges obtained and the frontier molecular orbitals evaluated. The hydrogen bonding and the non-classical intermolecular interactions within the two frameworks were investigated using *Hirshfeld* surface analysis which indicated the presence of C—H…H—C, C—H···π, C—H···O, C—H···N, C—H···S and π···*lp* interactions as well as π···π stacking. Additionally, in order to understand the interacting binding sites of the two molecules with the bacterial *S. aureus* protein receptors, the studied compounds were *in silico* evaluated by molecular docking against tyrosyl-tRNA synthetase **1JIJ** and topoisomerase II DNA gyrase **2XCT** enzymes. The results revealed consequently potent antimicrobial efficacy through the formed hydrogen bonds, hydrophobic contacts, π-cation interactions and π…π stacking.

1. Introduction

Gram-positive methicillin-resistant Staphylococcus aureus (MRSA) is one of the most common antibiotic-resistant bacteria. It causes life-threatening bloodstream, surgical-site infections and pneumonia. This class of infection-causing bacteria cannot be controlled or killed by antibiotics and it is instead able to survive and even multiply in the presence of an antibiotic [1–6]. Despite the ongoing pharmaceutical research undertaken in order to respond to the clinical need to develop new antibiotics, the antimicrobial resistance (AMR) continues to be challenging and the spread of antibiotic-resistant bacteria poses a substantial threat to public health worldwide [7–10]. Therefore, a growing clinical need for the ability to continuously develop new potent antimicrobial compounds is to be urgently considered to fight clinical diseases and to equipotently inhibit multiple bacterial targets [11–13].

In fact, tyrosyl-tRNA synthetase (TyrRS) belongs to the aminoacyl-tRNA synthetases which play a key role in the catalysis of the amino acids' condensation with their respective tRNA to form charged tRNAs [14]. In addition, the inhibition of these enzymes affects the cell growth by altering the protein biosynthesis process. Thus, TyrRS represents an attractive target enzyme to develop new potent antibacterial agents [15,16]. On the other hand, type II DNA topoisomerases are vital

* Corresponding author.
E-mail addresses: direm.amani@univ-khenchela.dz, amani_direm@yahoo.fr (A. Direm).

https://doi.org/10.1016/j.inoche.2022.109779
Received 12 May 2022; Received in revised form 24 June 2022; Accepted 17 July 2022
Available online 19 July 2022