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Seleno-L-cystine and Vanillin Schiff's base: Synthesis, Reaction Mechanism and Biological activity

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In this study, the new Schiff base bearing Se–Se bond and vanillin core in the structure was synthesized from the naturally occurring amino acid selenocystine and vanillin as an aldehyde counterpart. Taking into account the fact that synergy of different pharmacophores in one molecular structure could bring interesting biological properties, the synthetized compound was screened for the antimicrobial activities with respect to their minimum inhibitory concentracion (MIC) values for different bacteria and fungi cultures, as well as for binding interactions with deoxyribonucleic acid (DNA) and bovine serum albumin (BSA). Furthermore, the additional quantum chemical calculations and molecular docking simulations were performed for the better insight into detailed mechanism of Schiff base-formation and mode of its biological activities. It has been observed that among tested bacterial and fungal strains, the best antimicrobial activity was displayed for the *Staphylococcus aureus*, while the fluorescence quenching experiments have revealed that compound possesses binding affinity towards both BSA and DNA.

Introduction

The presence of selenium, as an essential micronutrient, in different organic scaffolds is beneficial for the establishment of interesting biological properties, starting from the antimicrobial,[1] anticancer,[2,3] antioxidant[4] to the antiviral activities.[5] The selenium is present in the active site of many enzymes (glutathione peroxidase (GPx)) and takes key roles in different metabolic processes, such as immune response, thyroid hormone metabolism and antioxidative defense.[6,7] In biological systems, selenium is mostly present in the form of selenomethionine, Se-methyl-selenocysteine, selenocysteine and selenocystine.[8]

Selenocystine is a naturally occurring selenoaminoacid, as well as a dimeric oxidation form of selenocysteine and selenium analogue of cystine. Due to the pronounced stability under physiological conditions (in comparison to the selenocysteine), this compound is also suitable for the different in vitro and in vivo biological investigations. The special attention has been given to the anticancer activity-essays of the selenocystine, and many studies demonstrated its potential as an effective agent against human melanoma, breast, liver, lung, and cervical cancer cells.[9–14] The development in this area can be attributed to higher sensitivity of cancer cells to selenocystine in comparison to the healthy cells,[11] as well as to the unique chemical features of the diselenide bond present in this amino acid.[15,16] Selenocystine also possesses anti-hemolytic activity due to the ability to reduce peroxyl radicals and hydroperoxides.[17] One recent study has revealed the potential of selenocistine as a drug against respiratory tract infections causing bacterial biofilms.[18] In addition, selenocystine is an excellent starting point for the design and synthesis of novel stable diselenide bond-containing proteins that could be also submitted to the different biomedical screenings.[19] Beside the use of selenocystine for the protein synthesis, there is literature evidence which suggests the modification of its original core for the improvement and/or modification of its pharmacological performances.[20,21]

The introduction of organoselenium moiety into other pharmacologically active scaffolds is today a recognizable concept for the creation of compounds with prominent medical application. This model has been successfully applied for the synthesis of organoselenium-modified steroids,[22] coumarins,[23] vitamins,[24] pyridines,[25] where the synergy between selenium functionality and other pharmacophore in one molecule is almost always leading to the establishment of improved biological activities and/or features necessary for the application under physiological conditions.

From the other side, the Schiff bases, condensation products of the amines and aldehydes involving the imine group in the structure, represent an important family of organic compounds with promising application in the medical field.[26,27] The Schiff bases are especially valued as convenient ligands for the preparation of transition metal complexes.[28]

Bearing the above in mind, we envisioned that modification of selenocystine, by the introduction of an imine pattern in its

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