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«АКТУАЛЬНІ ПИТАННЯ СУЧАСНОЇ МЕДИЦИНИ ТА ФАРМАЦІЇ»

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antioxidant drug candidates. The present results of antioxidant activity have shown that the synthesized compounds demonstrated considerable antioxidant effects. When compared with existing antioxidants, some our compounds were found to be more potent. Further optimization of the structure to improve biological activity is currently in progress.

COMPUTATIONAL CHEMISTRY STRATEGIES FOR ANTIOXIDANT ACTIVITY INVESTIGATION

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Mounting research has been performed in the recent decades focusing on natural and low-molecular-weight synthetic antioxidants discovering as key molecules that control oxidative damage and its pathway to disease [1, 2].

Oxidative stress is a phenomenon resulting from the imbalance between oxidation-reduction processes, in particular, the formation and accumulation reactive oxygen species (ROS) and reactive nitrogen species (RNS) in cells and tissues, and the ability of the antioxidant defence system of the organism to eliminate these by-products [3]. Oxidative stress develops under the influence of external or internal factors and leads to oxidative modification of biomolecules, in particular lipids, proteins and DNA [4]. One- and two-electron oxidation-reduction reactions, as an integral part of aerobic metabolism, often lead to free radicals' *in vivo* formation [5]. Molecular oxygen reduction processes include the stepwise single electron reduction of O_2 results in such ROS generation as superoxide anion radical ($O_2^{\bullet-}$), hydrogen peroxide (H_2O_2) and hydroxyl radical ($HO^{\bullet}$) [6]. H_2O_2 is produced as a result of two-electron O_2 reduction. Reactive nitrogen species include mainly nitric oxide ($NO^{\bullet}$), nitrogen dioxide ($NO_2^{\bullet}$) and peroxynitrite ($ONOO^-$), as well as non-radicals such as

nitrous acid HNO_2 and N_2O_4 (dinitrogen tetroxide) [7]. Fig. shows some possible pathways of ROS and RNS transformations.

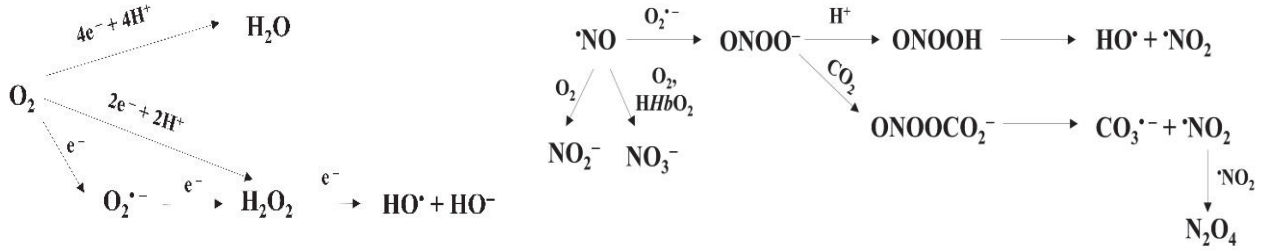

Fig. Some possible pathways of ROS and RNS transformations.

At lower concentrations ROS/RNS have beneficial effects and indulged in different physiological processes such as redox regulation, mitogenic responses, cellular signaling pathways, and an immune function while at a higher level, these reactive species generate nitrosative and oxidative stress.

In modern research the two main types of antioxidants are distinguished: (1) the primary antioxidants, or free radical scavengers, which are able to break the chain reaction; (2) the secondary, or preventive, antioxidants, for which the action mechanisms may include the deactivation of metals, inhibition of lipid hydroperoxides by interrupting the production of undesirable volatiles, the regeneration of primary antioxidants, and the elimination of singlet oxygen [8]. The methods of the antioxidant capacity determining are commonly classified into two main groups, based on the reaction mechanisms involved in free radicals' reduction process: (a) hydrogen atom transfer (HAT) reactions; and (b) transfer reactions of a single electron (SET) [9].

The process of new synthetic antioxidants discovery as therapeutics is a complicated process which includes the identification of bioactive chemical structure, the elucidation of the mechanism of action using different *in vitro* and *in vivo* model systems, and the toxicological evaluation. Thus, one of the most promising pathways is to optimize the use of computational chemistry strategies in resolving and discovering antioxidant activity [10].

The most used computational chemistry strategies employed over the past five years to investigate the antioxidant activity, may be categorized into five aspects: electronic structure analysis, thermodynamic analysis, kinetic analysis, interaction analysis, and bioavailability analysis.

- Electronic structure analysis strategies giving the electron distribution characteristics have been often used to explain and predict the antioxidant activity, pinpoint the reaction sites, and elucidate the molecular mechanisms. Among molecular electronic parameters which are calculated and analysed within this approach, are: Frontier Molecular Orbitals (FMOs), Molecular Electrostatic Potential (MEP/ESP), Global Chemical Reactivity Descriptors (GCRDs) (the energy involved in extracting and donating electrons from a molecule, as ionization potential, IP, and

electron affinity, EA, respectively), *etc*.

- Thermodynamic Analysis approach includes the related enthalpies of different antioxidant mechanisms assessment in the processes of direct free radicals' scavenging.

- Kinetic Studies are primarily focused on calculating rate constants using the Gibbs free energy of activation found with transition state theory (TST).

- Interaction Analysis is commonly based on Quantum Theory of Atoms in Molecules (QTAIM), a mathematically rigorous theory concerning atomic region division, bonding analysis, and charge analysis. Its theoretical foundation relies entirely on the properties and geometric characteristics of electron density. Currently, QTAIM analysis stands out as one of the most powerful tools for analysing intramolecular hydrogen bonds. Molecular Docking (MD) and Molecular Dynamics Simulations (MDS) MD can rapidly simulate molecular interactions such as hydrogen bonds, electronic interaction, and Van der Waals interaction.

- Bioavailability Analysis include computational assessment of physico-chemical properties of substances which are essential for their solubility, lipophilicity, distribution and membrane permeability. These properties include: (1) dissociation constant (pKa), which determines the charge of the compound in solutions and thus influences for example solubility, protein binding, hydrogen-bound formation, and biological activity; (2) Partition coefficient LogP and Distribution coefficient LogD; (3) Polar Surface Area (PSA), which is used to predict membrane permeability.

Therefore, it is important to integrate the results of computational chemistry studies into the framework of antioxidants' development and discovery to obtain a comprehensive profile that accurately reflects antioxidant mechanisms and parameters influencing antioxidant activity enhancement.

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MOLECULAR DOCKING STUDIES OF 3*H*-THIAZOLO[4,5-*b*]PYRIDINE DERIVATIVES AS POTENTIAL LIPOXYGENASE INHIBITORS

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Nowadays the discovery of effective antioxidant agents among low-molecular-weight organic molecules is a recent problem that requires new methodological approaches implementation, while it is also the society relevant task [1]. Both thiazole and pyridine scaffolds are of the highest priority in modern medicinal chemistry [2, 3]. Numerous reports concerning variety biological effects possessed by thiazolopyridine derivatives have been currently published including their discovery as potent antioxidant agents [4].

One of the antioxidant action mechanisms can be exerted through the inhibition enzymes' activity which are responsible for reactive oxygen species (ROS) producing, thereby reducing oxidative stress. The objective of the precent study was