PHARMACIA

Pharmacia 71: 1–8
DOI 10.3897/pharmacia.71.e133114

Research Article

Hydrazide-hydrazones as novel antioxidants - in vitro, molecular docking and DFT studies

Emilio Mateev[1], Muhammed Tilahun Muhammed[2], Ali Irfan[3], Shubham Sharma[4], Maya Georgieva[1], Alexander Zlatkov[1]

1 *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University – Sofia, Sofia, Bulgaria*
2 *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Suleyman Demirel University, Isparta 32260, Turkey*
3 *Department of Chemistry, Government College University Faisalabad, Faisalabad 38000, Pakistan*
4 *Department of Chemistry, GLA University, Mathura, India*

Corresponding author: Emilio Mateev (e.mateev@pharmfac.mu-sofia.bg)

Received 7 August 2024 ♦ **Accepted** 20 September 2024 ♦ **Published** 16 October 2024

Citation: Mateev E, Tilahun Muhammed M, Irfan A, Sharma S, Georgieva M, Zlatkov A (2024) Hydrazide-hydrazones as novel antioxidants - in vitro, molecular docking and DFT studies. Pharmacia 71: 1–8. https://doi.org/10.3897/pharmacia.71.e133114

Abstract

The pathogenesis of many diseases, such as obesity, depression, cancer, cataract, and neurodegenerative diseases, is related to the generation of reactive oxygen species (ROS). Structures possessing radical-scavenging properties act as antioxidants and they could prevent the progression of the aforementioned diseases. Therefore, the current work was focused on the resynthesis and the antioxidant evaluation of 13 hydrazide-hydrazones. Two *in vitro* tests - DPPH and ABTS, were applied for the determination of the antioxidant capacities. The free-radical scavenging assays displayed that the hydrazide-hydrazone synthesized after condensation with a salicylaldehyde (5b) is the most potent antioxidant. The *in vitro* evaluation through the ABTS test showed that the former structure has greater antioxidant properties compared with the used standard - Trolox (6-Hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid). In concentrations of 31 μM, the pyrrole-based structure showed 35.77% radical-scavenging effects. A possible binding conformation of the most active hydrazide-hydrazone in the active site of NADPH oxidase was visualised through docking simulations. The active amino acids involved in the stabilisation of the complexes were discussed. DFT studies demonstrated that 5b is a stable structure with good hydrogen and electron donating properties. Overall, the pyrrole-based hydrazide-hydrazone possesses promising antioxidant properties, however further *in vitro/in vivo* biological evaluations are required.

Keywords

Hydrazide-hydrazones, Antioxidants, Oxidative stress, Molecular docking, DFT

Introduction

The equilibrium between the antioxidant systems in the body and the generated free radicals is of great importance. Increased levels of the reactive oxygen species (ROS) formed in the mitochondria, could violate the balance and lead to generation of oxidative stress. The former could damage the living cells (Bozkurt et al. 2020). Some examples of oxygen-centered free radicals are superoxide ($O_2^{\cdot}$), peroxyl ($ROO^{\cdot}$), alkoxyl ($RO^{\cdot}$), hydroxyl ($HO^{\cdot}$), and nitric oxide ($NO^{\cdot}$). Importantly, the generation of ROS is reported to be related with the pathogenesis of some diseases, such as obesity, depression, cancer, cataracts, and neurodegenerative diseases etc. (Bolduc et al. 2019). Antioxidants are natural or synthetic chemical molecules that protect the cells from the oxidative damage caused by free radicals. Thus,

Copyright *Mateev E et al.* This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

PENSOFT

structures with antioxidant effects could prevent the progression of the aforementioned diseases (Jasril et al. 2021).

There are many pharmacologically active molecules with a hydrazide-hydrazone fragment which could be formed after a synthetic reaction between a hydrazide and aldehydes/ketones. Ligands with a hydrazide-hydrazone groups are experimentally tested as antimicrobials, antiseptics, antidepressants, antituberculars, antifungals, anti-inflammatories, antivirals, antiprotozoal, and others (Shabeeb et al. 2019). Currently, drugs such as Isoniazid (antitubercular), isocarboxazid (antidepressant), nitrofurazone (antimicrobial) are registered compounds comprising a hydrazide-hydrazone moiety (Fig. 1). Importantly, recent findings have shown that the molecules with a hydrazide-hydrazone fragment act as antioxidants (Pallapati et al. 2020).

Thus, the aim of this work was to identify novel antioxidants comprising a hydrazide-hydrazone moiety. The radical-scavenging capacities of the title compounds were accessed through the reliable *in vitro* antioxidant assays - DPPH and ABTS. Subsequent molecular docking simulations in the active site of NADPH, which is heavily involved in the oxidative stress cycle, were carried out. To observe the energy minimised conformation of the most active hydrazide-hydrazone, DFT calculations were introduced.

Materials and methods

Synthesis of hydrazide-hydrazones

All of the synthetic steps were previously reported by our research group (Mateev et al. 2024). The reagents were obtained from Merk without further purification. The resynthesised compounds were confirmed by IR spectroscopy.

DPPH assay

The antioxidant capacities of the resynthesised hydrazide-hydrazones were initially tested with the DPPH in vitro assay. DPPH (2,2- diphenyl-1-picrylhydrazyl) is a stable free radical which gives an intensive violet colour when dissolved in a solvent. Therefore, the radical-scavenging capacities of the organic compounds can be measured with UV/VIS. The absorption maximum is at 515 nm. In the current work the standard protocol reported by Brand-Williams et al. was followed (Brand-Williams et al. 1995). Briefly, the title compounds were dissolved in methanol to form three different concentrations 31–250 μM, followed by the addition of 1 mL methanol solution of DPPH (1 mmol/L). Each reaction mixture was incubated for 30 min in a dark room. Three measurements for each sample were carried out. Trolox was used as a standard. The percentile inhibition of the tested samples was calculated by the following formula (1):

$$DPPH_{scavenging\ activity} = Abs_{control} - Abs_{sample} / Abs_{control} \times 100\% \quad (1)$$

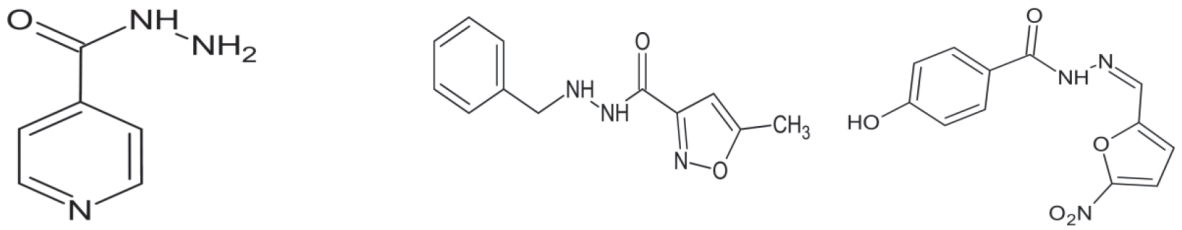
Where $Abs_{control}$ is the absorbance of DPPH radical in methanol and Abs_{sample} is the absorbance of DPPH radical solution mixed with sample.

ABTS assay

The ABTS radical scavenging capacities of the hydrazide-hydrazones were measured according to a modified method of Arnao et al. (Arnao et al. 1996). The absorbance was measured at λ = 734 nm. The stable radical cation ($ABTS^{+\bullet}$) was generated by mixing 7 mmol/L of ABTS and 2.4 mmol/L of potassium persulphate. The solution was allowed to react for 14 hr in the dark at room temperature. 1 ml of the ABTS working solution was reacted with the hydrazide-hydrazones for 15 minutes. Thereafter, the absorbance was measured. Trolox was used as a standart. The inhibition percentage was calculated applying the same formula as the DPPH assay.

Molecular docking studies

The molecular docking calculations were performed in the active site of NADPH oxidase with the docking module of Schrödinger - Glide (Schrödinger). The crystal structure of NADPH was downloaded from the PDB (PDB:2CDU) together with a co-crystallized ligand which was used to generate the grid space through the Receptor Grid Generation module. The hydrazide-hydrazone based antioxidants were drawn with 2Dsketch and prepared for the docking simulations with the module of Meastro - LigPrep. The crystal structure of NADPH was also prepared with the Protein Preparation module in Maestro. The extra precision module of Glide was used for the calculation of the energies and the complexes were visualised with the XP Visualized Maestro.



Isoniazid **Isocarboxazid** **Nitrofurazone**

Figure 1. Medications containing a hydrazide-hydrazone scaffold.

DFT calculations

DFT computation was performed via the Gaussian 09 program (Frisch et al. 2009). Compounds 5b and 5k were optimised through B3LYP/6311G^{++}(d,p) basis setup at the ground state. Thereafter, energy computation was performed with the same setup. The highest occupied molecular orbital (HOMO) energy and the lowest unoccupied molecular orbital (LUMO) energy values were fetched from the computation in atomic units (a.u.). These values were converted into electron volts (eV). Thereafter, the related parameters were computed with these values. Molecular electrostatic potential (MEP) and frontier molecular orbital (FMO) analysis were then performed after visualisation was undertaken via GaussView 5.0 (Dennington et al. 2008; Muhammed and Aki-Yalcin 2024).

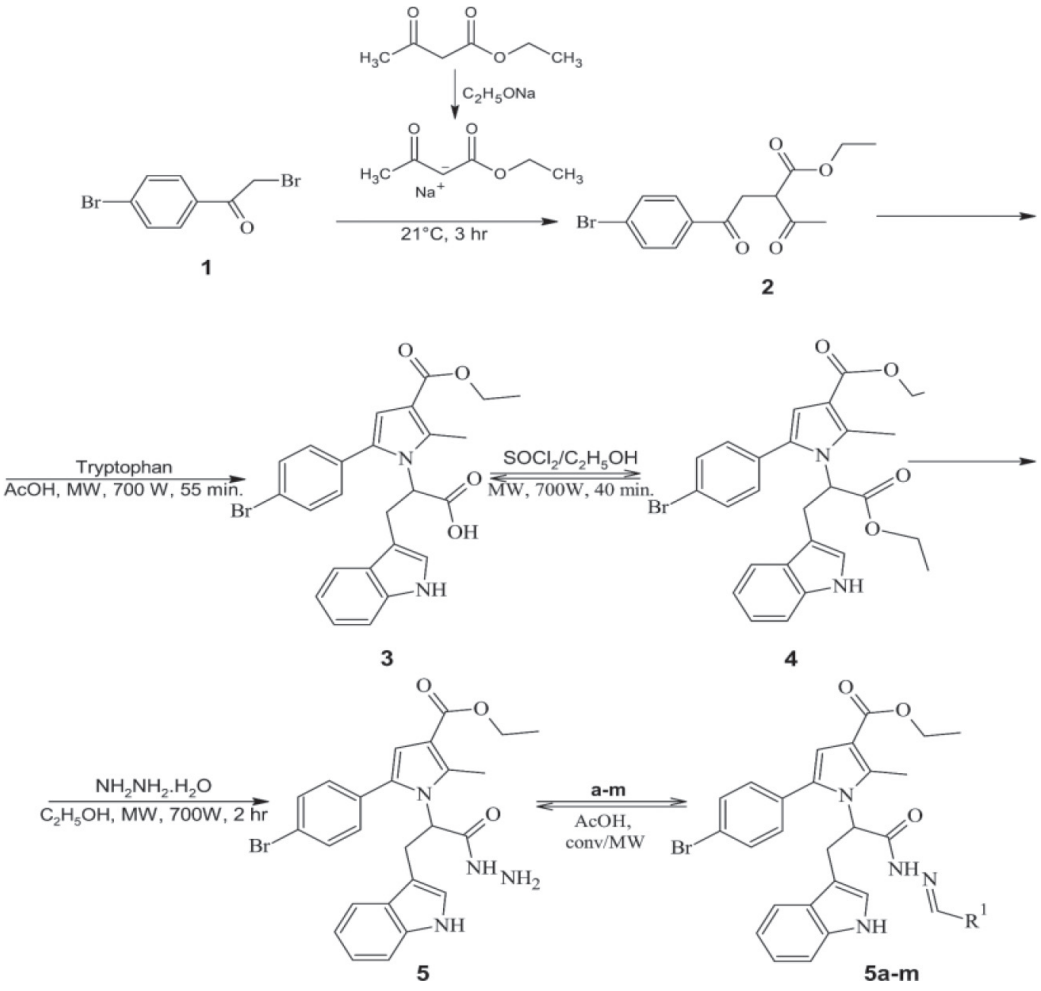
Results and discussion

Synthesis of hydrazide-hydrazones

Several recent works noted the antioxidant potential of the hydrazide-hydrazone moiety (Amine Khodjaz and Boulebd 2020). Introducing electron-donating moieties was also considered as a potential approach for increasing the overall antioxidant effects. The antioxidant effects of the pyrrole ring were also discussed (Kundu and Pramanik 2020). Moreover, the presence of a tryptophan ring in molecules with good antioxidant properties directed us in including the former ring in the final structures. Considering the discussed research works, we resynthesised a series of pyrrole-based hydrazide-hydrazones with a subsequent test for their radical-scavenging activities. The synthesis of the title compounds was previously reported by our research group (Mateev et al. 2024) (Scheme 1) (Fig. 2). The final reaction step was optimised by using microwave irradiation which led to fast reaction times and good yields. Essentially, microwave irradiation leads to high temperature which is related to the direct heating effect (Shi and Hwang 2003). Importantly, all hydrazide-hydrazones were prepared for 30 seconds with excellent yields when the MW radiation was employed in the process. The infrared spectra of the synthesised compounds were compared with the previously reported data.

Antioxidant assays

The antioxidant effects of the synthesized hydrazide-hydrazones were assessed through DPPH and ABTS testing.



Scheme 1. Synthesis of the pyrrole-based hydrazide-hydrazones.

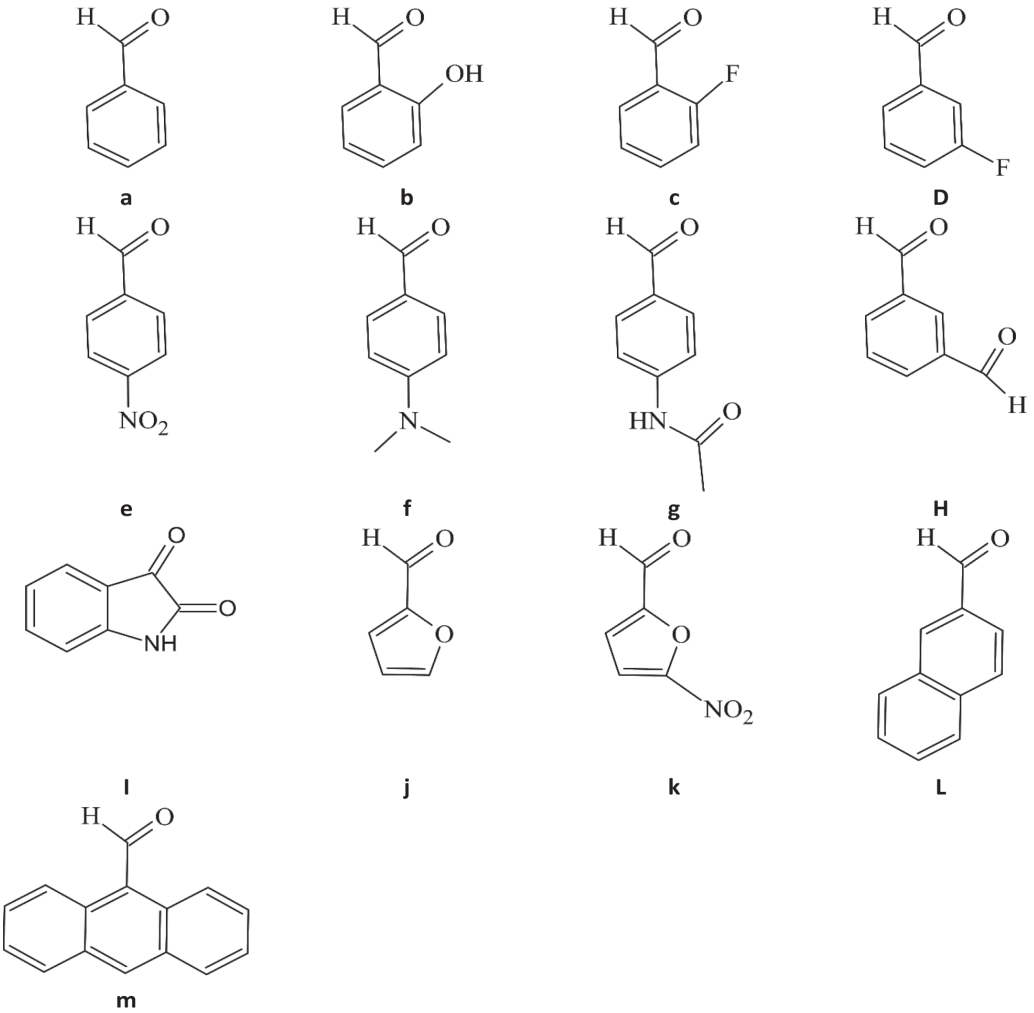


Figure 2. Aldehydes used for the condensation reactions.

DPPH assay

The radical scavenging properties during the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay is mainly associated with the hydrogen donating capacity of the tested compounds which could be detected spectrophotometrically with a decrease of the absorbance at 517 nm. For the current testing three concentrations were used (ranging from 31 to 250 μM). The DPPH radical scavenging effects of compounds 5a-m are displayed in Fig. 3. Trolox was used as a standard.

The most active compound after evaluations with the DPPH test was the hydrazide-hydrazone 5b, which contains a hydroxyphenyl group. In the highest applied concentration (250 μM), the former structure showed 61.27% radical-scavenging property. Using the same concentration, Trolox displayed 92.94% effect which is considerably higher. Interestingly, none of the other compounds demonstrated any radical scavenging activities after using the DPPH test. The main hypothesis is that the presence of a hydroxyl group causes the good antioxidant effect of 5b. Recently reported paper confirms that the introduction of a hydroxy moiety enhances the DPPH performance of the compounds (Yamauchi et al. 2024).

ATBS assay

During the ABTS test, the tested antioxidants could neutralise the ABTS cation and the change could be detected by the discoloration of the initial colour. Decreased absorbance at 734 nm indicates that the tested structures are with good antioxidant capacities. The ABTS radical-scavenging test of the hydrazide-hydrazones is provided in Fig. 4.

Overall, all of the applied hydrazide-hydrazone showed moderate to excellent ABTS radical scavenging properties. The most active compound was the hydrazide-hydrazone condensed with salicylaldehyde - 5b, which showed better results compared with the applied standard Trolox. It was noted that 5k also demonstrated moderate antioxidant activity and it could be further evaluated. At concentrations of 250 μM, 125 μM, and 31 μM, compound 5b displayed inhibition of 90.49, 60.44, and 35.77%, respectively. Numerous studies have shown that the introduction of a hydroxyl functional group leads to significantly enhanced antioxidant effects (Chen et al. 2020). Moreover, both tests showed different results and it was concluded that the ABTS test is more suitable for the tested hyrazide-hydrazones.

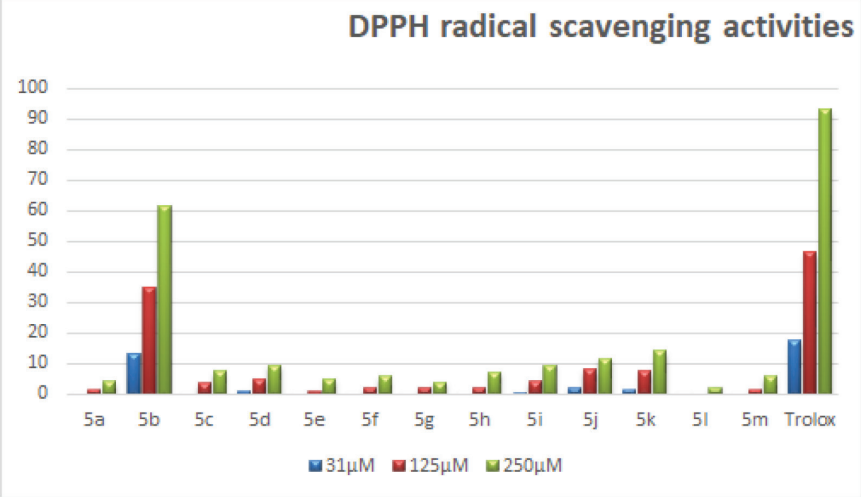


Figure 3. DPPH radical capacity of the hydrazide-hydrazones at concentrations 31, 125 and 250 µM. Standard deviation (SD) (n = 3).

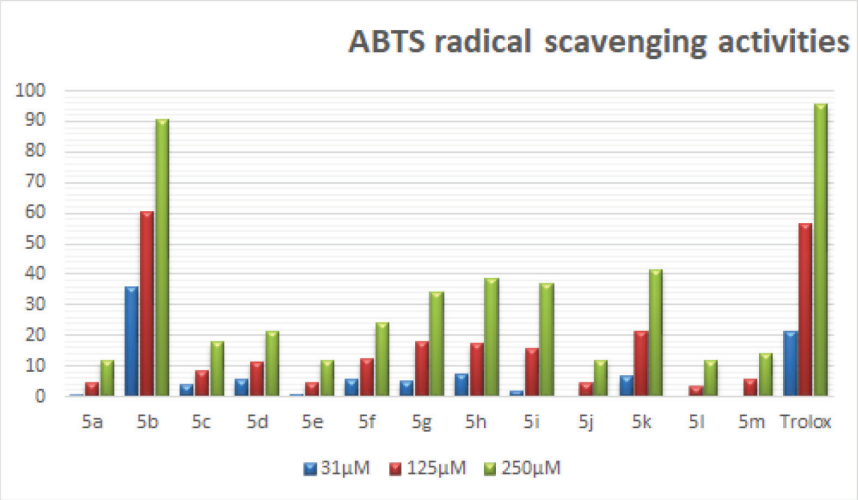


Figure 4. ABTS radical capacity of hydrazide-hydrazones at concentrations 31, 125 and 250 µM. Standard deviation (SD) (n = 3).

The differences could be discussed with the ability of the ABTS test to examine both hydrophobic and hydrophilic compounds (Thaipong et al. 2006; Floegel et al. 2011). An article reported by Nayak et al. discussed that the tryptophan fragment increases the antioxidant effects (Nayak et al. 2016). Interestingly, the implementation of a tryptophan ring in the current study led to good results only after the utilisation of the ABTS test, however the DPPH assay showed little to none antioxidant effects of the applied molecules.

Molecular docking studies

NADPH oxidases (NO) are enzymes that are mainly involved in the transfer of electrons to molecular oxygen. That process leads to the generation of reactive oxygen species (Tarafdar and Pula 2018). Moreover, it is noted that NO generates ROS during the metabolism of arachidonic acid. Therefore, the inhibition of NO lowers the oxidative stress and the maintenance of the redox homeostasis (Costa et al. 2018). A confirmation of the latter statement is noted in several papers that have reported the *in silico* simulations of ligands with free-radical scavenging activity in the active site of NO (Irfan et al. 2021). Thus, the *in silico* simulations in the current paper were conducted in the active pocket of NO (PDB code: 2CDU). Only the best antioxidant according to the DPPH and ABTS assays was tested - 5b. The calculated interactions are given in both 2D and 3D panels (Fig. 5).

Two hydrogen bonds between 5b and Phe245 were observed. Moreover, the distances were optimal - 1.95 and 2.15 Å which shows the stability of the formed bonds. Lys187 was introduced into p-cation bonding with the benzene ring of the tryptophan ring, therefore it could be hypothesized that the tryptophan moiety enhances the antioxidant properties of 5b. In addition, the active residues Tyr188, Phe245, Tyr296, Ile297, Pro298, Leu346 and Ala349 participated in hydrophobic interactions with 5b. Overall, the formation of two stable hydrogen bonds with the hydroxyl group in the salicylaldehyde moiety demonstrates the importance of –OH function group for the formation of low energy complexes with NO.

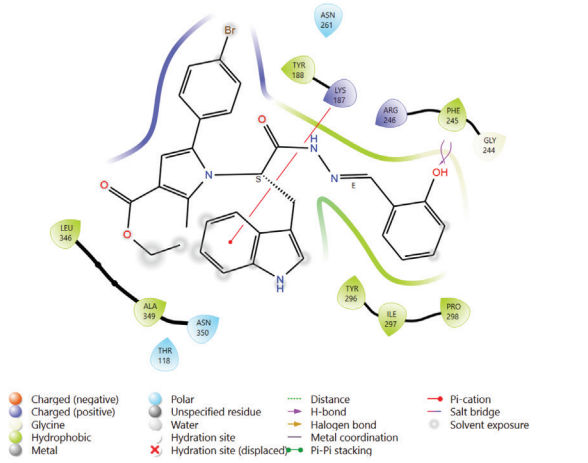
DFT studies

MEP Appraisal

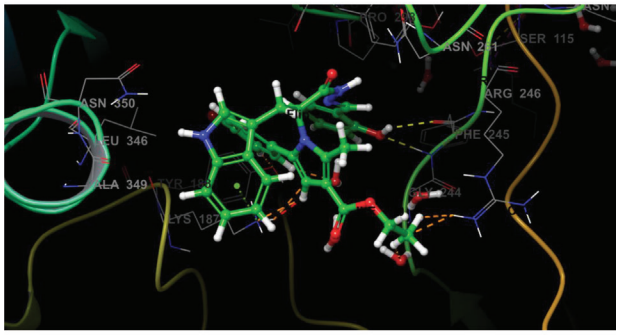
The electrophilic and nucleophilic reactive sites of a compound are determined by the MEP surface distribution. A negative electrostatic potential is correlated to a higher electron density site that is ready to attract protons. These sites on a compound are mainly illustrated in red. Yellow coloured sites also depict such regions but with a lower proton attraction relative to the red coloured sites. A positive electrostatic potential is correlated to a lower electron density site that is prone to electron attraction and proton repulsion. These sites on the MEP map of a compound are mainly illustrated in blue. The green coloured sites on the MEP map of a compound illustrate the neutral site with zero electrostatic potential (Mavvaji et al. 2023). The oxygen of the carbonyl functional in the carboxylate of compounds 5b and 5k was coloured in red in their MEP maps. The oxygen of the hydroxyl substituent on the benzylidene ring of compound 5b was inside the yellowish site and near to the red coloured site of its MEP map. Similarly, oxygens' of the nitro substituent on the furan ring of compound 5k were inside the yellowish site and near to the red coloured site of its MEP map (Fig. 5). The above listed nucleophilic oxygen atoms of the two compounds could act as electrophilic attack sites. This data suggested that the oxygen in these sites would facilitate the formation of hydrogen bonds in the interaction of the compounds with a target. The hydrogens on the nitrogen of the indole ring in compounds 5b and 5k were in the blue coloured site of the compounds' MEP maps. Additionally, light blue coloured sites were observed in the MEP maps of the two compounds, especially around the hydrazide bridge (Fig. 6). These blue vicinities depict the nucleophilic attack sites of the compounds (Kinaytürk 2024).

FMO Analysis

The DFT calculation gave the HOMO and LUMO energies of compounds 5b and 5k. Based on these values, related electrical parameters of the compounds were computed. The computed parameters were harnessed to figure out the reactivity and stability of the compounds. The HOMO energy is correlated to the electron donating capacity of an optimized structure. The LUMO energy is the reflection of the ability of the optimised compound for gaining electrons. The energy gap between the LUMO and HOMO energies (ΔE) is crucial in understanding the relative stability and reactivity of compounds (Kınaytürk et al. 2023). The energy gap value of compound 5b was found to be higher than the value of 5k implying a higher stability and a lower reactivity for it (Table 1). The ionization potential shows the energy required to remove electron from a compound's ground state. A compound with a higher ionization potential needs a higher energy to remove electrons from its ground state. So, this compound will be resistant for donating electrons. In this computation, compound 5k gave a higher ionization energy suggesting a higher



A



B

Figure 5. Visualised intermolecular interactions between 5b and the active site of NO. A. 2D interaction; B. 3D interaction.

energy requirement for electron donation. Compound 5k had a lower HOMO energy relative to compound 5b (Table 1). Hence, the electron donating capacity of compound 5k was found to be lower. The HOMO energy and the ionization potential results suggested that compound 5k would show a lower electron giving capacity. A higher electron affinity implies a higher electron absorbing capacity and a lower electron giving capacity. In this study, compound 5b had a lower electron affinity (Table 1). This in turn shows a higher electron giving capacity for it. This was reflected in its higher HOMO energy value (Table 1).

The relative hardness and softness of compounds are used to compare the stability and reactivity of the compounds. The hardness of a compound reflects its resistance for electron distribution implying a higher stability (Muhammed et al. 2023). In this study, compound 5b gave a higher hardness value than that of 5k (Table 1). Hence, compound 5b is anticipated to be more stable. This result was in line with the result of evaluation via energy gap. On the other hand, a higher softness reflects a higher propensity for reactivity. In this study, compound 5k gave a higher softness value (Table 1). Hence, compound 5k is expected to have a higher propensity for reactivity. In short, the DFT study revealed that 5b would be more stable and 5k would be more reactive.

The HOMO and LUMO orbitals of compound 5b were distributed differently. The HOMO orbitals were mainly concentrated around the indole heterocyclic ring. On the

Table 1. The computed electrochemical properties obtained from the DFT study.

Parameters	5b	5k
E_{total}	-117,842.961	-121,298.451
E_{HOMO}	-5.412	-5.530
E_{LUMO}	-1.781	-3.321
ΔE	3.631	2.209
Ionization potential (IP= -E_{HOMO})	5.412	5.530
Electron affinity (A = -E_{LUMO})	1.781	3.321
Chemical potential (μ = -(I + A)/2)	-3.597	-4.256
Hardness (η = (I-A)/2)	1.816	1.105
Mulliken electronegativity (^{x} = (I + A)/2) [8]	3.597	4.256
Softness (S = 1/2η)	0.275	0.452
Electrophilicity index (ω = μ^2/2η) [9]	3.558	8.187
Maximum charge transfer (ΔN_{max} = (I + A)/2(I-A)) [10]	0.990	1.926

other hand, the LUMO orbitals were mainly concentrated around the 2-hydroxybenziledenehydrazinyl group of the compound (Fig. 6). Some degree of similarity between the orbital distributions of compounds 5b and 5k was observed. In this respect, the HOMO orbitals of compound 5k were mainly concentrated around the indole ring. On the other hand, the LUMO orbitals were mainly concentrated around the 5-ntirofuran heterocyclic ring (Fig. 7).

Conclusion

13 hydrazie-hydrazones were tested for their antioxiant capacities. Analysing the radical scavenging effects of the resyntheized compounds revealed some common characteristics. The introduction of a hydroxyl functional group was crucial for the overall antioxidant properties of the hydrazide-hydrazones. The docking simulations displayed that the tryptophan ring is involved in a stable H-bond in the active pocket of NADPH. The formation of two stable hydrogen bonds with the hydroxyl group in the salicylaldehyde moiety demonstrated the importance of the -OH function group for the low energy complex with NO. The DFT studies showed that compound 5b is stable and with low reactivity. Moreover, the structure possesses good electron donating ability. Therefore, 5b could be used for future *in vitro* and *in vivo* evaluations.

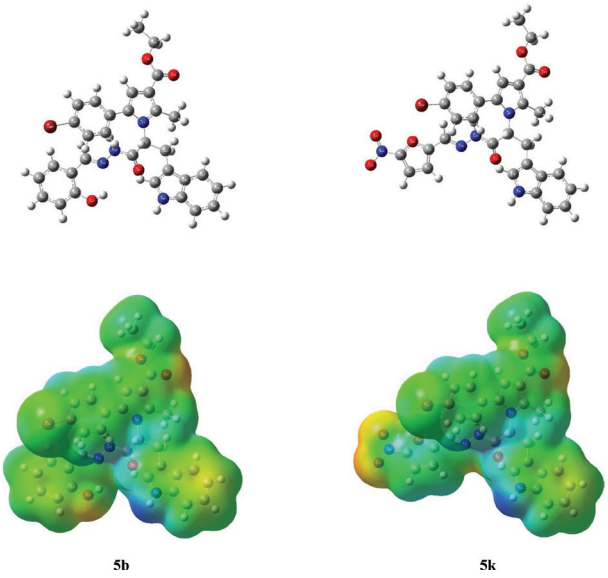


Figure 6. Optimised structures (upper panel) and MEP distribution maps (lower panel) of 5b and 5k.

Funding

This study is financed by the European Union-Next-GenerationEU, through the Nation-al Recovery and Resilience Plan of the Republic of Bulgaria, project № BG-RRP-2.004-0004-C01.

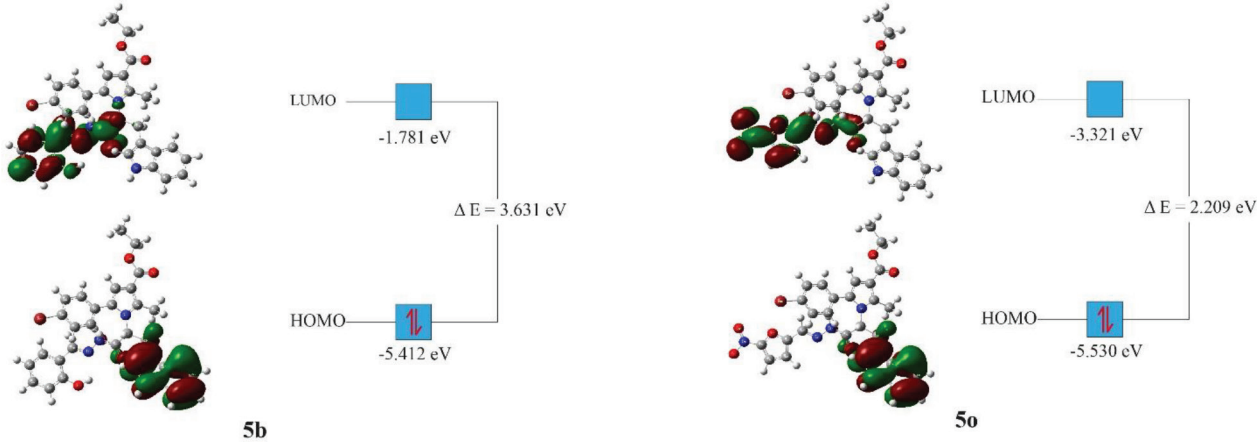


Figure 7. HOMO-LUMO orbitals of compounds 5b and 5k with corresponding energy values at B3LYP/6311G++(d,p) basis set.

References

Amine Khodjaz I, Boulebd H (2020) Synthesis, biological evaluation, theoretical investigations, docking study and ADME parameters of some 1,4-bisphenylhydrazone derivatives as potent antioxidant agents and acetylcholinesterase inhibitors. Molecular Diversity 25(1): 279–290. https://doi.org/10.1007/s11030-020-10064-8

Arnao B, Cano A, Hernández-Ruiz, García-Cánovas, Acosta M (1996) Inhibition byl-Ascorbic Acid and Other Antioxidants of the 2,2`-Azino-bis(3-ethylbenzthiazoline-6-sulfonic Acid) Oxidation Catalyzed by Peroxidase: A New Approach for Determining Total Antioxidant Status of Foods. Analytical Biochemistry 236(2): 255–261. https://doi.org/10.1006/abio.1996.0164

Bolduc J, Collins J, Loeser R (2019) Reactive oxygen species, aging and articular cartilage homeostasis. Free Radical Biology and Medicine 132: 73–82. https://doi.org/10.1016/j.freeradbiomed.2018.08.038

Bozkurt E, Sıcak Y, Oruç-Emre E, Iyidoğan K, Öztürk M (2020) Design and Bioevaluation of Novel Hydrazide-Hydrazones Derived from 4-Acetyl-N-Substituted Benzenesulfonamide. Russian Journal of Bioorganic Chemistry 46(5): 702–714. https://doi.org/10.1134/S1068162020050052

Brand-Williams W, Cuvelier E, Berset C (1995) Use of a free radical method to evaluate antioxidant activity. LWT - Food Science and Technology 28(1): 25–30. https://doi.org/10.1016/S0023-6438(95)80008-5

Chen J, Yang J, Ma L, Li J, Shahzad N, Kim CK (2020) Structure-antioxidant activity relationship of methoxy, phenolic hydroxyl, and carboxylic acid groups of phenolic acids. Scientific Reports 13 10(1): 2611. https://doi.org/10.1038/s41598-020-59451-z

Costa S, Ramos S, Costa L, Brasil B, Silva D, Ferreira B, Borges S, Campos M, Macêdo C, Santos D (2018) An In Silico Study of the Antioxidant Ability for Two Caffeine Analogs Using Molecular Docking and Quantum Chemical Methods. Molecules (Basel, Switzerland) 23(11): 2801. https://doi.org/10.3390/molecules23112801

Dennington J, Keith R, Millam T (2008) GaussView 5.0.

Floegel A, Kim D-O, Chung J, Koo I, Chun K (2011) Comparison of ABTS/DPPH assays to measure antioxidant capacity in popular antioxidant-rich US foods. J. Food Compost Anal 24(7): 1043–1048. https://doi.org/10.1016/j.jfca.2011.01.008

Frisch M, Trucks G, Schlegel H, Scuseria G, Robb M, Cheeseman J, Scalmani G, Barone V, Petersson G, Nakatsuji H, Li X, Caricato M, Marenich A, Bloino J, Janesko B, Gomperts R, Mennucci B, Hratchian H, Ort J, Fox D (2009) Gaussian 09, 53–54.

Irfan A, Imran M, Al-Sehemi AG, Shah A. T, Hussien M, Mumtaz W (2021) Exploration of electronic properties, radical scavenging activity and QSAR of oxadiazole derivatives by molecular docking and first-principles approaches. Saudi Journal of Biological Sciences 28(12): 7416–7421. https://doi.org/10.1016/j.sjbs.2021.08.049

Jasril, Juwiyatri E, Fauza N, Afriana N (2021) Synthesis, in vitro Antioxidant Activity, and Toxicity Evaluation of Hydrazone Derivatives Naphthalene-1-ylmethylene hydrazine. Journal of Physics: Conference Series 2049(1): 012050. https://doi.org/10.1088/1742-6596/2049/1/012050

Kinaytürk N (2024) Spectroscopic Characterization, DFT Calculation, and Docking Analysis for Understanding Molecular Interaction Mechanism of Propiconazole and DNA. Journal of Applied Spectroscopy 90: 1334–1345. https://doi.org/10.1007/s10812-024-01671-6

Kınaytürk N, Önem E, Oturak H (2023) Benzoic acid derivatives: Anti-biofilm activity in Pseudomonas aeruginosa PAO1, quantum chemical calculations by DFT and molecular docking study. Bulletin of the Chemical Society of Ethiopia 37: 171–181. https://doi.org/10.4314/bcse.v37i1.14

Kundu T, Pramanik A (2020) Expeditious and eco-friendly synthesis of new multifunctionalized pyrrole derivatives and evaluation of their antioxidant property. Bioorganic Chemistry 98: 103734. https://doi.org/10.1016/j.bioorg.2020.103734

Mateev E, Kondeva-Burdina M, Georgieva M, Mateeva A, Valkova I, Tzankova V, Zlatkov A (2024) Synthesis, Biological Evaluation, Molecular Docking and ADME Studies of Novel Pyrrole-Based Schiff Bases as Dual Acting MAO/AChE Inhibitors. Scientia Pharmaceutica 92: 18. https://doi.org/10.3390/scipharm92020018

Mavvaji M, Muhammed M, Akkoc S (2023) Synthesis, Cytotoxic Activity, Docking and MD Simulation of N,N-Disubstituted New Benzimidazolium Salts. Chemistry Select 8: e202303053. https://doi.org/10.1002/slct.202303053

Muhammed MT, Kokbudak Z, Akkoc (2023) Cytotoxic activities of the pyrimidine-based acetamide and isophthalimide derivatives: an in vitro and in silico studies. Molecular Simulation, 1–11. https://doi.org/10.1080/08927022.2023.2202766

Muhammed M, Aki-Yalcin E (2024) Computational insight into the mechanism of action of DNA gyrase inhibitors; revealing a new mechanism. Current Computer-Aided Drug Design 20: 224–235. https://doi.org/10.2174/1573409919666230419094700

Pallapati K, Mutchu R, Khandapu K, Vanga R, Varala R, Bollikolla B (2020) Synthesis of Novel Gabapentin Scaffold Derived Hydrazide-hydrazones for Potential Antimicrobial agents and Antioxidants. Chemistry Africa 3(4): 881–888. https://doi.org/10.1007/s42250-020-00184-x

Shabeeb I, Al-Essa L, Shtaiwi M, Al-Shalabi E, Younes E, Okasha R, Abu Sini M (2019) New Hydrazide-hydrazone Derivatives of Quinoline 3-Carboxylic Acid Hydrazide: Synthesis, Theoretical Modeling and Antibacterial Evaluation. Letters in Organic Chemistry 16(5): 430–436. https://doi.org/10.2174/1570178616666181227122326

Shi S, Hwang Y (2003) Microwave-assisted wet chemical synthesis: advantages, significance, and steps to industrialization. Journal of Minerals and Materials Characterization and Engineering 02(02): 101–110. https://doi.org/10.4236/jmmce.2003.22009

Thaipong K, Boonprakob U, Crosby K, Cisneros-Zevallos L, Hawkins Byrne D (2006) Comparison of ABTS, DPPH, FRAP, and ORAC assays for estimating antioxidant activity from guava fruit extracts. J. Food Compost Anal 19(6–7): 669–675. https://doi.org/10.1016/j.jfca.2006.01.003

Tarafdar A, Pula G (2018) The Role of NADPH Oxidases and Oxidative Stress in Neurodegenerative Disorders. International Journal of Molecular Sciences 19(12): 3824. https://doi.org/10.3390/ijms19123824

Yamauchi M, Kitamura Y, Nagano H, Kawatsu J, Gotoh H (2024) DPPH Measurements and Structure—Activity Relationship Studies on the Antioxidant Capacity of Phenols. Antioxidants 13: 309. https://doi.org/10.3390/antiox13030309