

Synthesis, biological evaluation, and molecular docking of benzhydrazide derivatives

Emilio Mateev¹, Stefan Kostov¹, Shubham Sharma², Ali Irfan³, Alexandrina Mateeva¹,
Maya Georgieva¹, Alexander Zlatkov¹

¹ Department of Pharmaceutical chemistry, Faculty of Pharmacy, Medical University - Sofia, 2 Dunav str., 1000 Sofia, Bulgaria

² Department of Chemistry, GLA University, Mathura, Uttar Pradesh, India

³ Department of Chemistry, Government College University Faisalabad, Faisalabad, 38000, Pakistan

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

Received 13 May 2025 ♦ Accepted 21 May 2025 ♦ Published 27 June 2025

Citation: Mateev E, Kostov S, Sharma S, Irfan A, Mateeva A, Georgieva M, Zlatkov A (2025) Synthesis, biological evaluation, and molecular docking of benzhydrazide derivatives. Pharmacia 72: 1–8. <https://doi.org/10.3897/pharmacia.72.e158825>

Abstract

In the pursuit of discovering and developing compounds with antioxidant and other biological activities, we designed, synthesized, and evaluated 10 hydrazide-hydrazone derivatives of 4-hydroxybenzohydrazide (ohbh1-10) as potential antioxidants. The compounds were synthesized using a Milestone FlexiWave microwave reactor, which significantly reduced reaction times and improved product yields. The radical-scavenging activities of the synthesized derivatives were assessed through DPPH and ABTS assays, revealing moderate antioxidant activity compared to the standard antioxidant, Trolox. To explore their potential biological applications, molecular docking simulations were performed to evaluate the binding affinities of the hydrazide-hydrazones within the active sites of monoamine oxidase B (MAO-B) and acetylcholinesterase (AChE). The *in silico* studies indicated that ohbh10 could act as a dual inhibitor of MAO-B and AChE. Additionally, ADME predictions for ohbh10 demonstrated favorable pharmacokinetic properties, including good blood-brain barrier (BBB) permeability and gastrointestinal absorption. Future work will focus on introducing additional hydroxyl groups into the molecular framework to enhance radical-scavenging properties. Furthermore, the molecular docking results will be validated through *in vitro* experiments to confirm the dual inhibitory potential of ohbh10 against MAO-B and AChE.

Keywords

4-hydroxybenzhydrazide, hydrazide-hydrazones, antioxidants, molecular docking

Introduction

Hydrazides are a class of medications often used in the treatment of various conditions, including tuberculosis, hypertension, and bacterial infections. They are typically derived from hydrazines and contain a hydrazide group ($-\text{CONHNH}_2$). In recent years, molecules containing this moiety have been thoroughly examined

to have potential antioxidant effects, more specifically compounds such as isonicotinyl benzohydrazide, benzohydrazide Schiff bases, and even pyridine benzohydrazide derivatives. They all act as potent antioxidants due to their ability to chelate metals and scavenge free radicals (Carreiras and Marco-Contelles 2024).

Some notable pharmacologically active compounds containing the benzohydrazide moiety include isoniazid

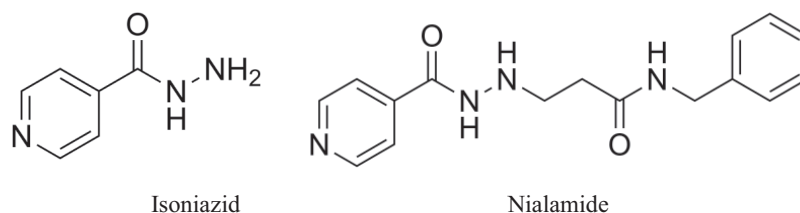


Figure 1. Medications containing a benzhydrazide scaffold.

and nialamide (Fig. 1) (Hu et al. 2017). The hydrazide moiety in isoniazid is crucial for its mechanism of action, as modifications to this group can significantly impact its pharmacological properties. Nialamide, another compound featuring the benzohydrazide scaffold, functions as a non-selective, irreversible monoamine oxidase inhibitor (MAOI). By inhibiting monoamine oxidase, nialamide increases the levels of key neurotransmitters such as serotonin, norepinephrine, and dopamine in the brain, which contributes to its antidepressant effects. In addition to these examples, the benzohydrazide scaffold serves as a core structure in a variety of other compounds exhibiting antibacterial, antifungal, anticancer, anti-inflammatory, and antioxidant activities, further underscoring its significance in medicinal chemistry (Hu et al. 2017).

Reactive oxygen species (ROS) are involved in both normal cellular processes and in various diseases. They are generated by several enzymes, including NADPH oxidase, xanthine oxidase, lipoxygenases, prostaglandin synthase, myeloperoxidase, and cytochrome oxidase, and are neutralized by antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, as well as antioxidant compounds like vitamins C and E, endogenous chelators, and glutathione (GSH). This creates a balance between antioxidants and pro-oxidants. While ROS are produced in response to normal physiological stimuli, their concentrations can become harmful if they rise beyond a certain threshold (Iliev and Georgieva 2024). Oxidative stress occurs when there is an imbalance between the production and buildup of reactive oxygen species (ROS) in cells and tissues and the cells' ability to remove these by-products. This imbalance arises from disruptions in the body's regulatory systems that maintain an equilibrium between pro-oxidants and antioxidants. The continuing accumulation of ROS plays a key role in the loss of neuronal cells seen in neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) (Dresen et al. 2023).

Considering the broad pharmacological actions of the benzhydrazide derivatives, as well as the involvement of oxidative stress in the pathogenesis of many diseases, the current work aims at the design and synthesis of 4-hydroxybenzhydrazide derivatives as potent antioxidants. Further, the interactions with major enzymes involved in the pathogenesis of neurodegenerative disease were displayed through molecular docking. The ADME profile of the most active antioxidant was examined through *in silico* calculations.

Materials and methods

Chemistry and synthesis

Available solvents and reactants were obtained from Merck without further purification. The synthesized compounds were confirmed by IR, ¹H-NMR, and MAS spectroscopy. The microwave-assisted reactions were carried out in a FlexiWave Milestone Lab Microwave reactor (equipped with fiber optic and IR sensors). The completion of the reactions was monitored by thin-layer chromatography (TLC). Infrared spectra were recorded on a Nicolet iS10 FT-IR spectrometer with a Smart iTR adapter (Thermo Fisher Scientific, USA). Mass spectra were obtained with a 6410 Agilent LCMS triple quadrupole mass spectrometer (LCMS) with an electrospray ionization (ESI) interface (Agilent Technologies, USA).

The title compounds were recently synthesized by Suzana et al. (Suzana et al. 2017; Suzana et al. 2019). However, no published studies have reported the synthesis of these compounds using a microwave reactor. To address this gap, the title compounds were synthesized in a Milestone Flexiwave microwave reactor to reduce reaction times and enhance final yields. The hydrazide-hydrazones (ohbh1-10) were prepared by reacting equimolar amounts (0.1 mmol) of 4-hydroxybenzohydrazide with 0.12 mmol of the respective carbonyl derivatives in the presence of a minimal quantity of glacial acetic acid as a catalyst. Upon completion of the reactions, as confirmed by thin-layer chromatography (TLC), the reaction mixtures were poured into cold water, and the resulting crystals were collected by filtration. The products were subsequently washed with hexane and recrystallized from an ethanol/water mixture. The structures of the synthesized hydrazide-hydrazones were confirmed by comparing their infrared (IR) and MAS spectra with previously reported spectral data.

Antioxidant effects

DPPH test

The DPPH test was carried out by following the Brand-Williams protocol (Brand-Williams et al. 1995). The compounds were tested in concentrations of 1 ml/mg and dissolved in DMSO. After the combination of the test samples with the stable radical DPPH, the mixtures were incubated for 30 min. in a dark room. Three measurements

were carried out. The absorption was measured with UV/Vis at 515 nm. Trolox was used as a standard. The percent-

tile inhibition of the tested samples was calculated by the following formula (1):

$$\text{DPPH scavenging activity} = \frac{\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}}{\text{Abs}_{\text{control}}} \times 100\% \quad (1)$$

Where $\text{Abs}_{\text{control}}$ is the absorbance of DPPH radical in methanol and $\text{Abs}_{\text{sample}}$ is the absorbance of DPPH radical solution mixed with sample.

ABTS test

The ABTS assay for the determination of the antioxidant effects of the 4-hydroxybenzhydrazone-hydrazones was carried out by a reported method by Arnao et al. (Arnao et al. 1996). The stable radical cation (ABTS^{•+}) was generated by mixing 7 mmol/L of ABTS and 2.4 mmol/L of potassium persulphate. The solution was left in a dark room for 14 hr. 1 ml of the ABTS working solution was reacted with the hydrazide-hydrazones for 15 minutes. The absorbance was measured at $\lambda = 734$ nm. The inhibition percentage was calculated applying the same formula as the DPPH assay.

Molecular docking

Two docking studies were carried out on two enzymes—MAO-B (PDB:2V5Z) and AChE (PDB:4EY7). The active sites were detected by observing the active conformation of the co-crystallized ligands. The proteins were prepared by adding hydrogen bonds, removing non-active water molecules, and minimizing the protein structures by utilizing the “Protein preparation” module in Maestro. The 4-hydroxybenzhydrazides were prepared by generating ionization forms in physiological pH, adding hydrogen bonds, and minimizing the geometric structures with the OPLS4 force field.

Two docking modes of Glide were used—SP and XP docking. The extra precision module of Glide was used for the calculation of the energies, and the complexes were visualized with the XP Visualized Maestro.

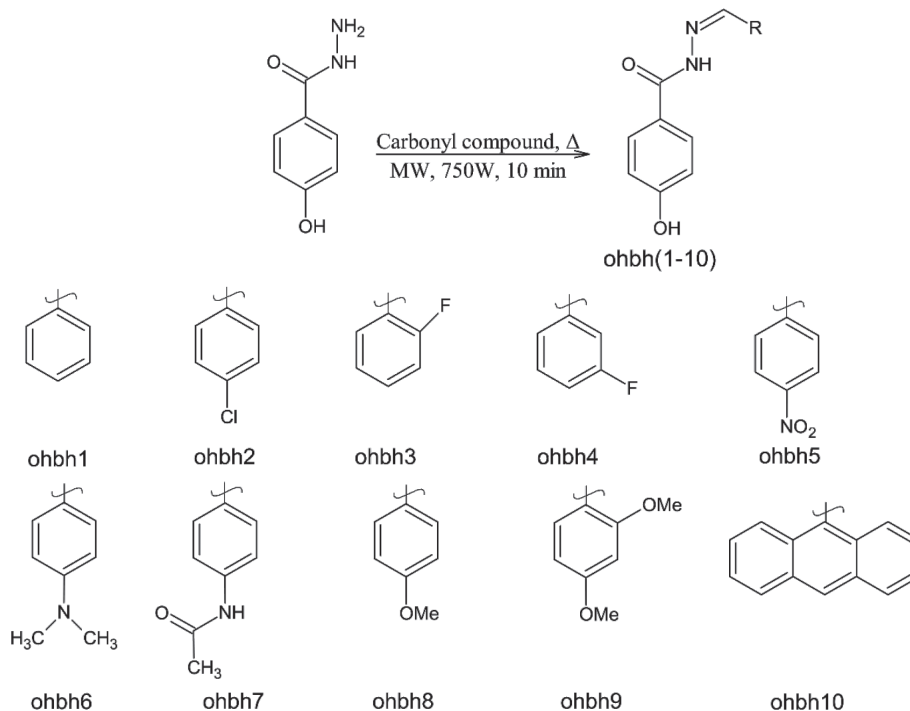
ADME studies

The Swiss ADME Internet server’s assistance (Daina et al. 2017) and computational studies of the newly synthesized compounds ohbh1-10 were performed to predict the molecular properties.

Results and discussion

Design and synthesis

The title 4-hydroxyhydrazide-hydrazones were designed by considering the major role of the -OH moiety in the oxidative stress. It was reported that polyphenol compounds and molecules comprising hydroxyl groups act as powerful antioxidants (Chen et al. 2020). Thus, the design was focused on the presence of the former moiety in the final compounds. Moreover, several papers discussed the positive role of the hydrazide-hydrazone fragment in the synthesized antioxidants (Şen and Şahin 2023). The synthesis of the title 4-hydroxybenzhydrazides was carried out through microwave-assisted condensation of carbonyl compounds with 4-hydroxybenzhydrazide (Scheme 1) (Suzana et al. 2017; Suzana et al. 2019).



Scheme 1. Microwave-assisted synthesis of 4-hydroxybenzhydrazide-hydrazones (ohbh1-10).

The microwave-assisted syntheses were completed in 10 minutes at 90 °C, and the final products were recrystallized from ethanol. The obtained compounds were elucidated through IR spectroscopy and MAS spectrometry. The microwave heating led to reduced reaction times—10 minutes for all compounds compared to recent studies of hydrazide-hydrazones of 4-hydroxybenzhydrazides (Oralgazy et al. 2023). Reaction times of 2 hr and refluxes for 5–6 h were discussed in some papers (Prachumrat et al. 2018; Maniak et al. 2020); thus, the reduction times after applying MW heating in this paper should be underlined.

Antioxidant assays

DPPH test

The antioxidant effects of the title 4-hydroxyhydrazide-hydrazones were initially observed by the DPPH assay. The obtained results are provided in Fig. 2.

Interestingly, all of the tested derivatives showed moderate radical-scavenging capacities in the range of 31% to 46% at a concentration of 1 mg/ml. The most promising compound from the tested hydrazide-hydrazones was ohbh4, which was condensed with 3-fluorobenzaldehyde. The latter molecule showed 46% radical-scavenging capacity towards DPPH. Since all of the examined compounds displayed similar antioxidant properties, it could be hypothesized that the main functional group responsible for the observed results is the hydroxyl moiety (Yamauchi et al. 2024).

ATBS assay

As an additional test for the antioxidant capacities of the synthesized compound, an ABTS assay has been included. The results are provided in Fig. 3.

Overall, all of the applied hydrazide-hydrazones displayed moderate ABTS radical scavenging properties

slightly better compared to the DPPH test. The most active compound was the hydrazide-hydrazone condensed with 4-chlorobenzaldehyde—ohbh2. Compared to the standard, it could be noted that none of the molecules possess similar antioxidant properties to Trolox. Thus, the applied compounds possess moderate radical-scavenging properties.

Noticeably, the introduction of a hydroxyl group in the benzhydrazide core structure leads to enhanced and similar antioxidant properties of the examined compounds. Future studies will be focused on the introduction of additional hydroxyl moieties and their effect on the radical-scavenging capacities.

Molecular docking

The significance of the *in silico* studies has been examined by many recent papers (Iliev et al. 2023; Andonova et al. 2024). To observe the hypothetical binding affinities of the synthesized hydrazide-hydrazones in the active sites of MAO-B and AChE, molecular docking simulations were carried out. MAO-B and AChE are reported to be involved in the pathogenesis of Alzheimer's disease (Spandidos and Vassiliou 2014), and the experimental radical-scavenging properties of the compounds could also be beneficial for the progression of the neurodegenerative disease. The docking calculations were done with the Glide module of Schrodinger, and two scoring functions were used in order to acquire data that is more reliable. The docking scores for both enzymes are given in Table 1.

While both standard precision (SP) and extra precision (XP) docking scores were utilized, the XP mode in Glide is generally regarded as more reliable. This is because the XP algorithm employs a more rigorous and computationally intensive approach, resulting in more accurate and detailed predictions of ligand binding affinities. Although XP docking requires more processing time, its enhanced precision makes it preferable for

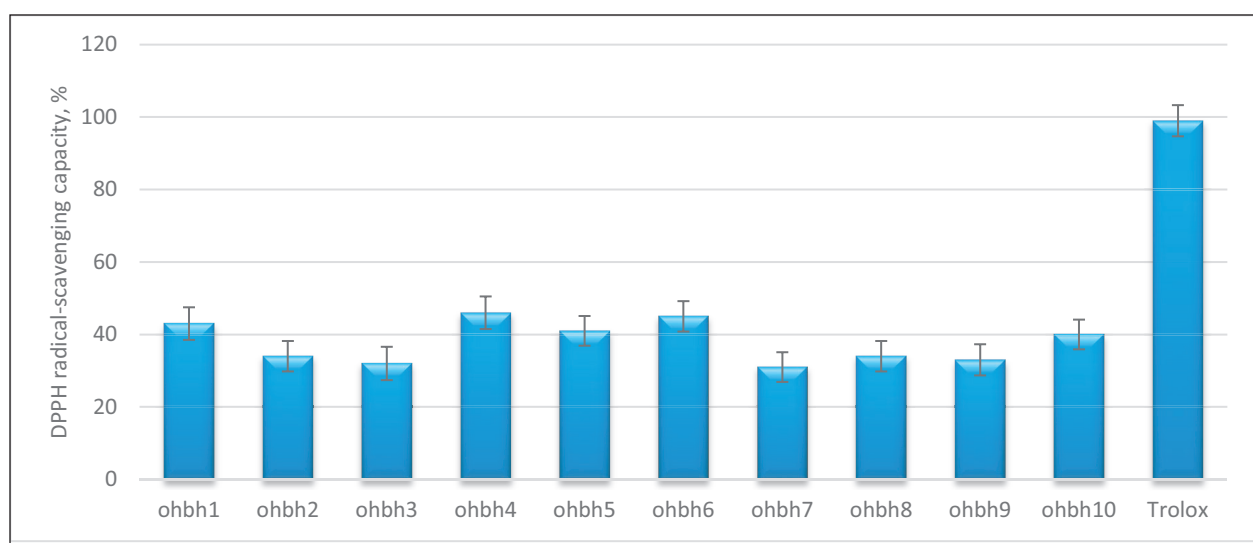


Figure 2. DPPH radical-scavenging capacity of 4-hydroxybenzhydrazide-hydrazone derivatives at concentrations of 1 mg/ml. Standard deviation (SD) (n = 3).

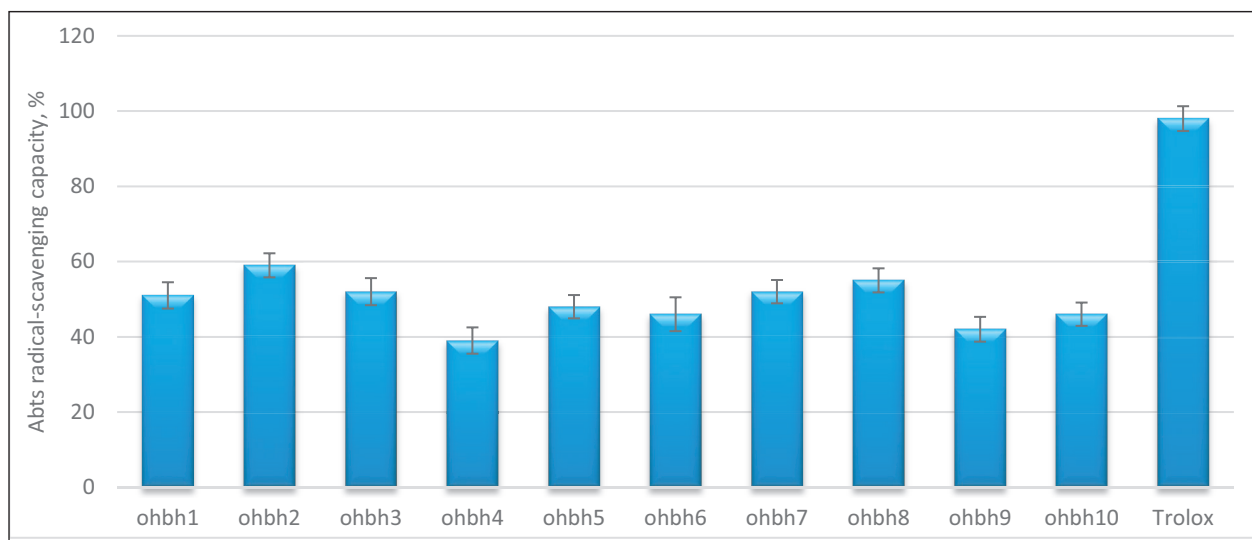


Figure 3. ABTS radical-scavenging capacity of 4-hydroxybenzhydrazide-hydrazone derivatives at concentrations of 1 mg/ml. Standard deviation (SD) (n = 3).

Table 1. Glide SP and XP docking scores in the active sites of MAO-B (PDB: 2V5Z) and AChE (PDB: 4EY7).

Compounds	MAO-B		AChE	
	Glide (SP score) kcal/mol	Glide (XP score) kcal/mol	Glide (SP score) kcal/mol	Glide (XP score) kcal/mol
ohbh-1	-9.51	-9.32	-7.09	-8.55
ohbh-2	-10.91	-10.41	-6.92	-7.05
ohbh-3	-9.73	-10.24	-7.56	-7.94
ohbh-4	-10.54	-10.32	-7.08	-7.16
ohbh-5	-8.14	-8.66	-6.88	-6.91
ohbh-6	-6.42	-5.87	-8.02	-8.26
ohbh-7	-5.04	-5.26	-6.71	-7.52
ohbh-8	-7.64	-7.91	-7.86	-8.01
ohbh-9	-8.17	-8.43	-7.59	-7.64
ohbh-10	-9.87	-9.94	-8.82	-9.02
*Safinamide	-14.72	-15.83	-	-
*Donepezil	-	-	-16.72	-18.72

*Reference compounds.

obtaining high-quality docking results. Therefore, the discussion of the docking results considered only the XP docking scores.

As observed, most of the compounds expressed moderate binding scores in both enzymes. The ligands possessing halogen atoms in the benzaldehyde moiety expressed the most promising binding scores in the active site of MAO-B (PDB: 2V5Z). The former hypothesis could be due to the electron-withdrawing capacity of the functional groups and the similarity to the well-known selective MAO-B inhibitor, Safinamide. The former has a fluorine atom in its structure. The hydrazide-hydrazones condensed with 4-acetamidobenzaldehyde and 4-dimethylaminobenzaldehyde displayed weak binding with the active amino acids in MAO-B, which is related to existing steric clashes. Importantly, none of the explored ligands expressed an XP docking score comparable to that of Safinamide. In the active site of AChE, the theoretical active inhibitor was the ligand including the anthracene ring in its structure—ohbh10. The noted results might be related to the similarity of ohbh10 with the chemical structure of tacrine

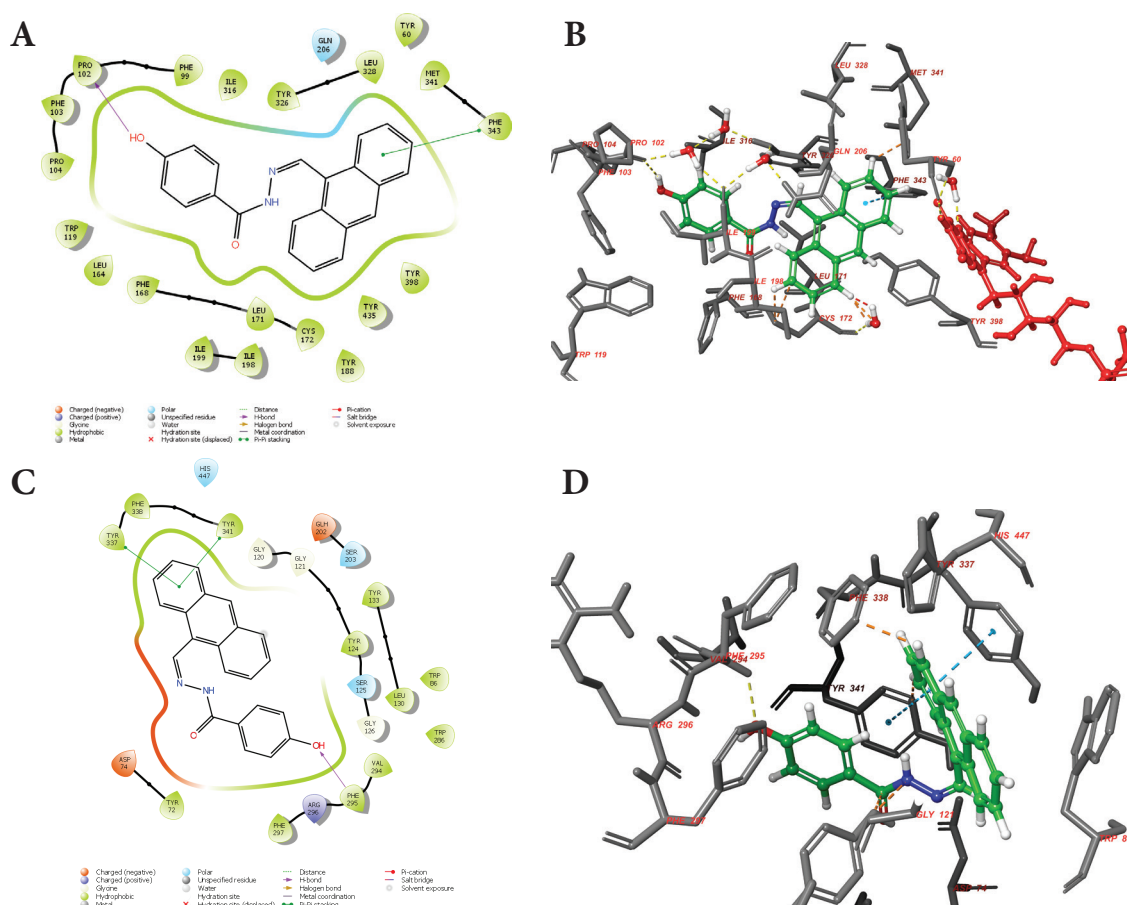
(1,2,3,4-tetrahydroacridin-9-amine). The rest of the applied molecules showed moderate capacity of inhibiting AChE with values in the range of -6.91 to -8.55 kcal/mol. Overall, the most prominent dual MAO-B/AChE inhibitor is ohbh10; thus, further exploration of the active amino residues involved in the stabilization interactions in both enzymes was conducted (Table 2).

3D and 2D panels of the intermolecular interactions of ohbh10 with MAO-B and AChE are provided in Fig. 4. The importance of the hydroxyl moiety is confirmed by the formation of two hydrogen bonds with active amino acids in both enzymes. In AChE the hydroxyl group formed an H-bond with Phe295, while in MAO-B Pro102 interacted with the -OH group. Interestingly, in the active site of MAO-B, the present co-factor FAD did not interact with the anthracene ring. The latter was situated in the “aromatic cage,” which includes Tyr398, Tyr435, and FAD. Phe343 from MAO-B was also involved in a stabilization with one of the aromatic rings from the anthracene moiety. As expected, the majority of the active amino acids in MAO-B were involved in hydrophobic interactions with ohbh10.

Table 2. Active amino acids involved in stabilization with the best dual inhibitor, ohbh-10.

Compound	H-bonds	π - π bonds	Hydrophobic interactions
ohbh10 AChE	Phe295 (2.26 Å)	Tyr337 (3.86 Å), Tyr341 (5.35 Å)	Tyr72, Trp86, Tyr124, Leu130, Tyr133, Val294, Phe295, Tyr337, Phe338, Tyr341
ohbh10 MAO-B	Pro102 (2.05 Å)	Phe343 (4.74 Å)	Tyr60, Phe99, Pro102, Phe103, Pro104, Trp119, Leu164, Leu167, Phe168, Leu171, Cys172, Ile198, Ile199, Ile316, Tyr326, Leu328, Met341, Phe343, Tyr398, Tyr435
*Safinamide MAO-B	Gln206 (1.87 Å, 1.97 Å), H ₂ O (1.61 Å)	Tyr326 (5.52 Å)	Tyr60, Trp119, Leu167, Phe168, Leu171, Cys172, Tyr188, Ile198, Ile199, Leu328, Phe343, Tyr398, Tyr435
*Denepezil AChE	H ₂ O (1.81 Å), Phe295 (1.98 Å)	Trp86 (4.15 Å), Tyr337 (3.73 Å), Phe338 (6.07 Å)	Tyr72, Trp86, Tyr124, Tyr133, Trp286, Leu289, Val294, Phe295, Phe297, Tyr337, Tyr338, Tyr341

*Reference compounds.

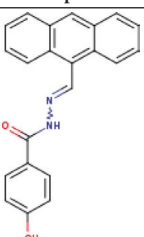
**Figure 4.** 2D and 3D panels of the major interactions of ohbh10 with the active sites of MAO-B and AChE (A, B - MAO-B; C, D - AChE). The ligand is depicted in green, and the FAD co-factor is given in red.

In silico ADME

An *in silico* study on the potential physicochemical properties and pharmacokinetic parameters of molecule ohbh10 was carried out. The respective data retrieved from the SwissADME evaluation process was organized in Table 3.

A majority of the developed drugs fail their clinical trials due to poor efficacy, toxicity, and overall pharmacokinetic profile. Two of the main pharmacokinetic descriptors in drug development are the penetration through the blood-brain barrier and the gastrointestinal absorption. To observe if the suggested lead compound possesses optimal values of the latter descriptors, a Brain Or Intestinal Estimated permeation method (BOILED-Egg) was carried out (Fig. 5) (Daina et al. 2017). The BOILED-Egg Model examines two physicochemical de-

Table 3. In silico ADME studies of ohbh10.

Compound	Pharmacokinetic parameters	
	WLogP	4.46
	CYP3A4 inhibitor	No
	CYP2C9 inhibitor	No
	Molecular weight	340.37 g/mol
	GI absorption	High
	P-gp substrate	No
	Synthetic accessibility	2.48
	TPSA	61.69 Å ²
	BBB permission	Yes

scriptors—lipophilicity (WLOGP) and polarity (TPSA). The lead structure synthesized in this work possesses optimal parameters for crossing the BBB and good gastrointestinal absorption. Thus, further *in vitro* experimental

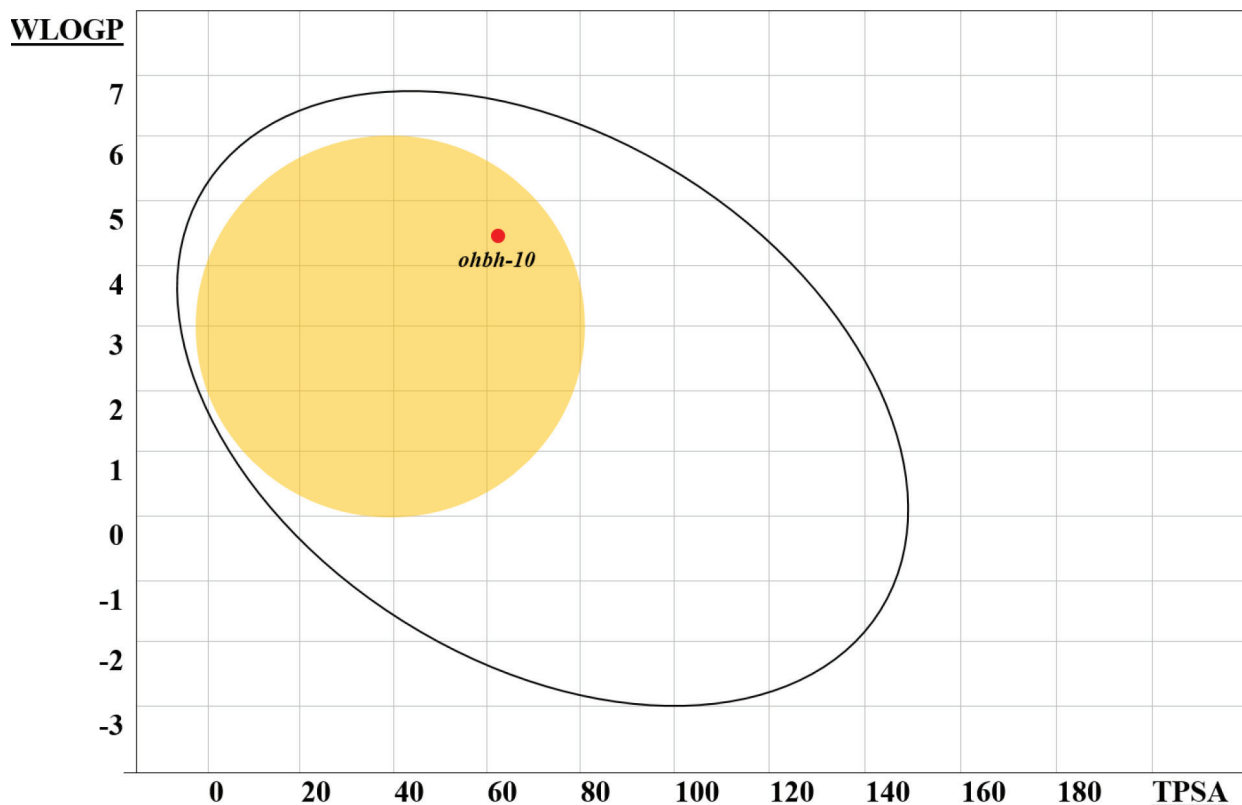


Figure 5. BOILED-Egg Model of ohbh10. The title molecule was depicted in red, the yellow zone is characterized by good BBB penetration, and the inner white zone is the passive gastrointestinal (HIA).

tests regarding the role of ohbh10 in treating neurodegenerative disease could be carried out.

Conclusion

The present study explores the microwave-assisted synthesis of ten hydrazide-hydrazone derivatives derived from 4-hydroxybenzohydrazide. Employing microwave irradiation led to a marked decrease in reaction times and enhanced yields compared to previously reported synthetic methods. The resulting compounds demonstrated moderate radical-scavenging activity relative to the standard antioxidant, Trolox. Notably, in silico molecular docking analyses indicated that ohbh10 may act as a dual inhibitor of both monoamine oxidase B (MAO-B) and acetylcholinesterase (AChE). To build upon these findings, future research should prioritize validating the computational predictions through comprehensive in vitro and in vivo experiments. Additionally, subsequent studies will focus on incorporating extra hydroxyl groups into the molecular structure to further investigate their influence on radical-scavenging efficacy.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Funding

This work was supported by the Council of Medical Sciences at the Medical University of Sofia Contract No. 146/29.05.2024.

Author contributions

All authors have contributed equally.

Author ORCIDs

Emilio Mateev <https://orcid.org/0000-0002-5885-7213>

Ali İrfan <https://orcid.org/0000-0002-8977-3303>

Alexandrina Mateeva <https://orcid.org/0000-0003-1905-7130>

Alexander Zlatkov <https://orcid.org/0000-0002-1695-8454>

Data availability

All of the data that support the findings of this study are available in the main text.

References

- Andonova V, Nikolova K, Iliev I, Georgieva S, Petkova N, Feizi-Dehnayebi M, Nikolova S, Gerasimova A (2024) Spectral Characteristics. In: *Silico Perspectives, Density Functional Theory (DFT), and Therapeutic Potential of Green-Extracted Phycocyanin from Spirulina*. International Journal of Molecular Sciences 25(17): 9170. <https://doi.org/10.3390/ijms25179170>
- Arnao MB, Cano A, Hernández-Ruiz J, García-Cánovas F, Acosta M (1996) Inhibition by L-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>
- Brand-Williams W, Cuvelier ME, Berset C (1995) Use of a free radical method to evaluate antioxidant activity. *Lebensmittel-Wissenschaft + Technologie* 28(1): 25–30. [https://doi.org/10.1016/S0023-6438\(95\)80008-5](https://doi.org/10.1016/S0023-6438(95)80008-5)
- Carreiras MDC, Marco-Contelles J (2024) Hydrazides as Inhibitors of Histone Deacetylases. *Journal of Medicinal Chemistry* 67(16): 13512–13533. <https://doi.org/10.1021/acs.jmedchem.4c00541>
- Chen X, Zhang Y, Wang J (2020) Structure-antioxidant activity relationship of methoxy, phenolic hydroxyl, and carboxylic acid groups in phenolic acids. *Scientific Reports* 10(1): 1–13. <https://doi.org/10.1038/s41598-020-59451-z>
- Daina A, Michielin O, Zoete V (2017) SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports* 7(1): 42717. <https://doi.org/10.1038/srep42717>
- Dresen E, Pimiento JM, Patel JJ, Heyland DK, Rice TW, Stoppe C (2023) Overview of oxidative stress and the role of micronutrients in critical illness. *JPEN. Journal of Parenteral and Enteral Nutrition* 47(S1): S38–S49. <https://doi.org/10.1002/jpen.2421>
- Hu Y-Q, Zhang S, Zhao F, Gao C, Feng L-S, Lv Z-S, Xu Z, Wu X (2017) Isoniazid derivatives and their anti-tubercular activity. *European Journal of Medicinal Chemistry* 133: 255–267. <https://doi.org/10.1016/j.ejmech.2017.04.002>
- Iliev I, Georgieva S (2024) Anti-aging components in the composition of anti-wrinkle cosmetic products: Antioxidants of natural and synthetic origin as active substances. *Varna Medical Forum* 13(1): 102–108. <http://dx.doi.org/10.14748/vmf.v13i1.10088>
- Iliev I, Georgieva S, Sotirova Y, Andonova V (2023) In silico study of the toxicity of hyperforin and its metabolites. *Pharmacia* 70(3): 435–447. <https://doi.org/10.3897/pharmacia.70.e107041>
- Maniak H, Talma M, Matyja K, Trusek A, Giurg M (2020) Synthesis and structure-activity relationship studies of hydrazide-hydrazones as inhibitors of laccase from *Trametes versicolor*. *Molecules* 25(5): 1255. <https://doi.org/10.3390/molecules25051255>
- Oralgazy A, Nurkenov SD, Fazylov SD, Satpaeva ZB, Seilkhanov TM, Turdybekov DM, Mendibayeva AZ, Akhmetova SB, Shulgau ZT, Alkhimova LE, Kulakov IV (2023) Synthesis, structure and biological activity of hydrazones derived from 2- and 4-hydroxybenzoic acid hydrazides. *Chemical Data Collections* 48: 101089. <https://doi.org/10.1016/j.cdc.2023.101089>
- Prachumrat P, Kobkeattawin T, Ruanwas P, Boonnak N, Laphookhieo S, Kassim MB, Chantapromma S (2018) Synthesis, crystal structure, antioxidant, and α -glucosidase inhibitory activities of methoxy-substituted benzohydrazide derivatives. *Crystallography Reports* 63(3): 405–411. <https://doi.org/10.1134/S1063774518030227>
- Şen B, Şahin E (2023) Design, synthesis, antioxidant and anticholinesterase activities of novel isonicotinic hydrazide-hydrazone derivatives. *Journal of Molecular Structure* 1324: 129–140.
- Spandidos DA, Vassiliou AG (2014) Monoamine oxidase inhibitors: Promising therapeutic agents for Alzheimer's disease. *Molecular Medicine Reports* 9(5): 1533–1541. <https://doi.org/10.3892/mmr.2014.2040> [Review]
- Suzana S, Isnaini I, Budiati T (2017) Synthesis, molecular docking and antimicrobial activity of N'-Benzylidene-4-Hydroxybenzohydrazide and N'-(4-Methoxybenzylidene)-4-Hydroxybenzohydrazide. *Research Journal of Pharmaceutical, Biological and Chemical Sciences* 8(2): 1360.
- Suzana S, Sulistyowaty M, Budiati T (2019) Synthesis, docking molecule study and antibacterial activity of N'-(4-Fluorobenzylidene)-4-Hydroxybenzohydrazide and N'-(4-Fluorobenzylidene)-4-Hydroxybenzohydrazide. *Journal of Physics: Conference Series* 1146: 012018. <https://doi.org/10.1088/1742-6596/1146/1/012018>
- 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(3): 309. <https://doi.org/10.3390/antiox13030309>