New hydrazones bearing fluoro-benzohydrazide scaffold: synthesis, characterization, molecular docking study, and anti-oxidant investigations

Article *in* Materials Today: Proceedings · July 2022

DOI: 10.1016/j.matpr.2022.06.335

4 authors, including:

Tanzeer Ahmad Dar
Annamalai University
3 PUBLICATIONS **1** CITATION
SEE PROFILE

Balasankar Thirunavukkarasu
7 PUBLICATIONS **59** CITATIONS
SEE PROFILE

Winfred Jebaraj
St. John's College, Palayamkottai
12 PUBLICATIONS **26** CITATIONS
SEE PROFILE

Materials Today: Proceedings xxx (xxxx) xxx

Contents lists available at ScienceDirect

Materials Today: Proceedings

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

New hydrazones bearing fluoro-benzohydrazide scaffold: synthesis, characterization, molecular docking study, and anti-oxidant investigations

Tanzeer Ahmad Dar [a], Balasankar Thirunavukkarasu [b,*], A. Ganapathi [b], Winfred Jebaraj [c]

[a] Department of Chemistry, Annamalai University, Annamalai Nagar 608002, Tamil Nadu, India
[b] Chemistry Section, FEAT, Annamalai University, Annamalai Nagar 608002, Tamil Nadu, India
[c] Department of Chemistry, St. John's College, Palayamkotti, Tirunelveli, Tamil Nadu, India

ARTICLE INFO

Article history:
Available online xxxx

Keywords:
4-fluorobenzohydrazide
Molecular docking
Anti-oxidant studies
1D- NMR range

ABSTRACT

N-Heterocycles are prime Skelton and have been taken as an important contrivance for the construction of competent bioactive molecules. This study intends to amalgamate, characterize, and anti-oxidant assessment of some piperdin-derived (E)-4-fluoro- analogs. We have amalgamated five new piperdin-derived (E)-4-fluoro- compounds. All the designed compounds were characterized using FT-IR, and 1D-NMR. Also, altogether the amalgams were inquired for their anti-oxidant actions in counter to innumerable free radicals. Compounds **Z3** and **Z4** spectacle outstanding anti-oxidant activities. The results flaunted that the electron-confer (donating) and electron-exodus (withdrawing) sets play a prime role in anti-oxidant actions of the compounds **Z (1–5)** respectively. A molecular docking study of the compound (Z1) demos that the innumerable ligands of the compound with a glide score value of −4.28 kcal/mol.

Selection and peer-review under responsibility of the scientific committee of 2022 International Conference on Recent Advances in Engineering Materials.

1. Introduction

Heterocyclic chemistry with N (nitrogen) heteroatom is nascent as some of the newest areas in the synthetic organic chemistry dome as its pervasive being of different bioactive natural compounds, synthetic intermediates, and pharmaceuticals [1]. A prevailing objective of chemical synthesis is to cultivate active and steadfast methods for the assembly of complex molecules [2]. The assortment of biologically energetic molecules has been thought of as a persuasive implement for the synthesis of chemical compounds with major bioactivity. Of specific concern to organic and medicinal chemists are nitrogen-containing heterocycles, which often originate in natural products [3,4], and therapeutic drugs [5,6]. Among N (nitrogen)-containing heterocycles, piperdin ring is the utmost common moiety in copious biologically active natural products and therapeutic agents, substantial attention has focussed on the improvement of general means and strategies for the synthesis of its by-products. Among the extensive variety of heterocycles that have been explored for developing the pharmaceutically important molecules, piperidin-4-one unveils numerous biological activities like analgesic, antibacterial, nervous system depressant, anti- fungicidal, and anti-oxidant activities. Besides the significant biological properties, piperdin-4-ones are useful building blocks in synthetic organic chemistry and are well documented[7,8].

The current effort was to explore the anti-oxidant activities in a piperdin loop having hydrazide moiety. In an endeavor to explore the conformations, natural profiles, and in precise, the anti-oxidant activity, a novel series of (E)-4-fluoro-Ń-(3-isopropyl-2,6-diphenyl piperidin-4-ylidene) benzohydrazides **Z (1–5)** were synthesized and characterized by ethereal techniques. The synthesized compounds were curtained for their antioxidant capabilities. The title compound was also curtained for molecular docking studies.

2. Experimental

2.1. General

2.1.1. Melting point determination

The melting point was taken in open glass capillaries on the SUNTEX melting point apparatus and was uncorrected.

* Corresponding author.
E-mail address: drtbalasankar1974@gmail.com (B. Thirunavukkarasu).

https://doi.org/10.1016/j.matpr.2022.06.335
2214-7853/
Selection and peer-review under responsibility of the scientific committee of 2022 International Conference on Recent Advances in Engineering Materials.

2.1.2. FT-IR ranges

FT-IR ranges were documented on an AVATAR 330.0 FT-IR spectrometer in the KBr pellets.

2.1.3. NMR ranges

Proton NMR (H^1) and C^{13} NMR ranges were noted on a Bruker Avance NMR spectrometer functioning 400.00 MHz for H^1 and 100.00 MHz for C^{13}. Elucidations for record Proton NMR (^1H) and ^{13}C NMR ranges were set by liquefying around 10.00 mg and 50.00 mg of the compounds, respectively, in 0.5 ml $CdCl_3$. The number of statistics points for ^1H and ^{13}C was at 16 K and 32 K, correspondingly. Altogether the dimensions were prepared by exhausting 5.00 mm NMR tubes.

2.1.4. Anti-oxidant activity

The anti-oxidant commotion of the synthesized compounds Z **(1–5)** was buttressed out on diverse sample meditations (w/v) by liquefying (120, 90.60, and 30) milligram of starch in 1.00 ml of ddH_2O (deionized water) monitored by ultrasonication for 23.0 min to endorse well intercourse. The fusion achieved was exploited for defining, unlike anti-oxidant assays.

2.1.4.1. 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) radical scavenging action. 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) action of compounds was stanch by the routine recommended by Ashwar et al. [9] with specific alterations. 5.00 ml of every taster of fluctuating concentrations was mixed with a 60.00 mm elucidation of 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) in CH_3OH (5.00 ml). The solution was vortexed for approximately 0.30 s and kept at 25.00 °C for 30–35 min in an obscure chamber. The transmittance of the subsequent elucidation was resolute at 517.0 nm using Ultraviolet -vis. spectrophotometer in the flaw of the outright, tocopherol was engaged +Ve control, liquefied in dd-H_20, 1-picryl-hydrazyl-hydrate-**2**,2-diphenyl scavenging ability was acquired with the given formulae:

$$\text{DPPH activity } (\%) = (1 - \text{As})/\text{Ac} * 100$$

Therefore "Ac" is the transmittance of the +Ve reaction control, and "As" is the transmittance of the case.

2.1.4.2. Metal chelating action. MC was considered bestowing to the way Shah et al. [10]. The transmittance of the ensuing solution was executed at the 20–25 °C (ambient temperature) in a flaw of utter at 650.00 nm and paralleled to $C_6H_8O_7$ (control). The Fe^{2+} chelation competency of every case was intended as a percentage chelating outcome through the given calculation:

$$\text{Chelating effect } (\%) = (\text{Ac} - \text{As})/\text{Ac} * 100$$

"Ac" is the transmittance of the +Ve control of reaction and "As" is the transmittance of the case.

2.1.4.3. Prohibition of LP (lipid peroxidation). This assessment was premeditated by the subsequent pattern by Shah et al. [10]. Polysaccharide (starch) suspension (00.5–1.00 ml) of fluctuating meditations was auxiliary to the $C_{18}H_{32}O_2$ (1.00 ml, 0.1 percent w/v), H_2O_2 (0.2 ml, 30.00 mm), $C_6H_8O_6$ (0.2 ml, 100.0 mm), and Fe $(NO_3)_3$ (0.2 ml, 20.00 mm). The solution was legitimate to the nurtured at 37.0 °C for 60 min. Afterward, the dissolution of the response was reinforced out by addition $C_2HCl_3O_2$ (0.5–1.00 ml, 1.0 % m/v), and the $C_4H_9N_2O_2S$ (1.00 ml, 1.00 m/v). Response blend spouts were preserved in a steaming water immersion for 20.0–25.0 min monitored by centrifugation at 600.00 rpm for 5.0–6.0 min. The filtrate was assembled and its transmittance was set at 530.00 nm in contradiction to blank and paralleled at EDTA (control).

Reticence was deliberation as percent by the subsequent chemical equation:

$$\% \text{ Inhibition} = \text{Ac} - \text{As}/\text{Ac} * 100$$

"Ac" is the transmittance of the +Ve control reaction whereas "As" is the transmittance of the case.

2.1.5. Molecular docking contemplate.

The subsequent technique stood operated for molecular docking contemplate. The molecule for docking discourse was secure via Schrodinger, LigPrep. The ion devours magnitudely sophisticated and consigned to apt of isomerization state at pH 7.00 ± 2.00. The solid point optimization has been reinforced with the help of the OPLS- 2005 pressure subject. The object protein InhA (*enoylacyl* and *carrier protein reductase*) from TB (*Tubercle bacillus)* was taken from the wwPDB (Protein id: 2NSD) and the vigorous site was selected. The lattice was apportioned by selecting the molecule as the middle of the network and then the network case was spawned by spreading evasion factors. The docking alteration has been ended using GLIDE, Schrodinger, and GLIDE XP techniques.

2.1.6. General procedure

2.1.6.1. Synthesis of 3-isopropyl-2r,6c-diphenylpiperdin-4-ones T (1–5). The parental 3-isopropyl-2r,6c-diphenylpiperidin-4-ones **T (1–5)** were synthesized through Mannich reaction by adopting literature methods [11]. A mixture of ketone (0.1 mol), dried $C_2H_7NO_2$ (0.1 mol), suitable benzaldehyde (0.2 mol) in C_2H_5OH (30 ml), and heat to bubbling carefully. It was kept at ambient temperature for 12–14 h. Dry ether (50 ml) was added by Conce. HCl (30 ml) and cooled. The precipitated HCl was filtered and washed with ethanol- ether (1:5) mixture repeatedly. Then, HCl was suspended in acetone and made alkaline using strong NH_4OH. On dilution with an excess of H_2O, the base was precipitated which was filtered, dried, and recrystallized from C_2H_5OH.

2.1.6.2. Synthesis of (E)-4-Fluoro-N′-(3-isopropyl-2r,6c-diphenylpiperidin-4-ylidene) benzohydrazides Z (1–5). 4-fluorobenzohydrazide (1.5 mmol), and appropriate piperdin-4-one (1.0 mmol) were dissolved in 30 ml CH_3OH along with 1.0–1.5 ml of CH_3COOH as a catalyst to get a clear solution. The reaction mixture was taken in a round bottom flask and refluxed for about 4–5 h [Scheme 1]. After completion of the reaction, methanol was removed by vacuum distillation. The separate (E)-4-fluoro-N′-(3-isopropyl-2r,6c-diphenyl piperidin-4-ylidene)benzo-hydrazide Z(1–5) were recrystallized from ethanol and chloroform in equivalent ratio. The purity of the compounds was checked by TLC plates.

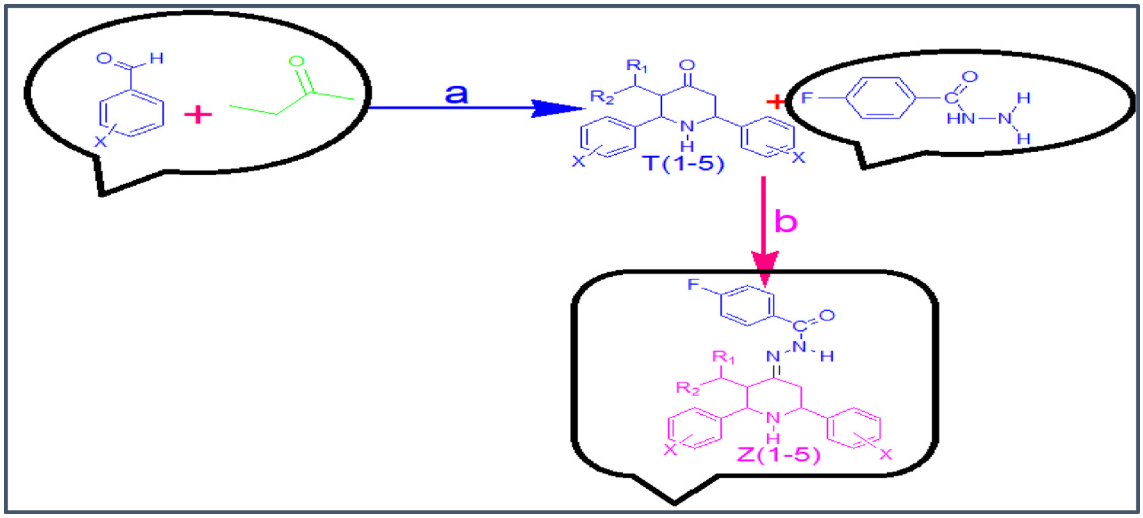
Reagents: (a) CH_3COONH_4, C_2H_5OH
(b) CH_3OH, CH_3COOH, 4 h, 60 °C

Sample code		R1	R2	X
T1	**Z1**	**CH_3**	**CH_3**	**H**
T2	**Z2**	**CH_3**	**CH_3**	**4-Cl**
T3	**Z3**	**CH_3**	**CH_3**	**4-OCH_3**
T4	**Z4**	**CH_3**	**CH_3**	**4-CH_3**
T5	**Z5**	**CH_3**	**CH_3**	**4-F**

Spectroscopic data for the complexes Z (1–5) are presented below:

(E)-4-fluoro-N′-(3-isopropyl-2,6-diphenylpiperidin-4-yli dene) benzohydrazide (Z1)

Light yellow powder, yield 83%, mp: 170–172 °C; **IR** (KBr, Vmax Cm^{-1}): 1660 (C═O), 1533 (C═), 3303 (N-H ring), 3167 (NH amide). **H^1 ranges** (400.00 MHz, $CdCl_3$, δ): 0.841, 01.032(doublet, 6-



Scheme 1.

protons, twice CH_3 at piperdin ring), 2.296 (mutiplet, CH at piperdin ring), 1.850 (singlet, H, N-H at piperdin ring), 2.877 (double, 1H, C-5, 1He), 2.757 (triplet, 1H, C-3, 1Ha), 2.856 (double-doublet, 1H, C5-1H), 04.190 (double, 1H, C-2,1Ha), 4.221(double,1H, C-6-1H-a), 7.253–7.475 (mutiplet, Aromatic – H), 10.545 (singlet, 1H, NH amide, NH). **C^{13} ranges** (400.00 MHz, $CdCl_3$-d6, δ): 19.39, 15.00 (twice CH_3 at piperdin ring), 37.40 (C-H at piperidine ring), 52.79 (C5), 57.101(C3), 61.2(C6), 67.86 (C2), 126.3–128.65 (Aromatic-C), 138.09–142.97 ipso- C, 166.45 (C-4 at Hydrazide ring), 163.40 C═N (C-9), 159.561 (NH-CO).

(E)-4-fluoro-N′-(2,6-bis(P-chlorophenyl)-3-isopropylpiperidin-4-ylidene) benzohydrazide (Z2)

White particles, yield = 93.0%, mp: 206–209 °C: **FT-IR spectra** (KBr, Vmax Cm^{-1}): 1651 (CO), 1546 (C═N), 3311(N-H ring), 3183 (NH amide).

H^1 ranges (400.00 MHz, $CdCl_3$, δ): 1.134, 1.138 (doublet, 6-H, twice CH_3 at piperidine), 2.289 (mutiplet, 1H, CH at piperidine ring), 1.546 (singlet, 1H, N-H at piperidine ring), 2.840(doublet, 1H, C-5-1H-a), 2.267(multiplet,1H,C-3-1H-a),4.186(doublet,1H,C-2-1Ha),4.242(doublet,1H,C6-1Ha),6.898–7.449(mutiplet,Aromatic-H), 9.897 (singlet, 1H, N-H amide). **C^{13}spectra** (400.00 MHz, $CdCl_3$, δ): 21.10, 21.30(twice CH_3 at piperidine), 30.11(C-H at piperidine), 35.49(C5), 57.39 (C3), 55.29(C6), 62.871 (C2), 128.39–135.30(Aromatic-C), 141.45–143.19(ipso- C), 162.17 (NHCO), 165.04(C-4 at hydrazide ring).

(E)-4-fluoro-N′-3-isopropyl-2,6-bis(P-methoxyphenyl)piperidine-4-ylidene) benzohydrazide (Z3)

White powder, Heed 73%, mp: 180–182 °C; **FT- IR** (KBr, Vmax Cm^{-1}): 1652 (O═C), 1548(CN), 3276(NH), 3174(NH amide). **H^1 data** (400.00 MHz, $CdCl_3$-d6, δ): 0.900, 0.950 (double, 6-H, 2*CH_3 at piperidine ring), 2.42(doublet, 1H, C-H at piperidine ring), 1.609(singlet, 1-H, N-H at piperdin ring), 1.889(singlet, 1-H, C-5,1-Ha), 3.279(singlet, 1H, C-5—1He), 3.850(singlet, 1H, C-2, -1Ha), 3.764(singlet, 6-H, -OCH_3),7.324–7.490(Aromatic-H), 10.239 (singlet, 1H, NH amide NH).

C^{13} spectra (400.00 MHz, $CdCl_3$-d6, δ): 15.11, 19.39(-CH_3 at piperidine ring), 32.35(C5), 51.79(-OCH_3), 61.00(C6), 66.80(C2), 126.65–135.12 (Aromatic-C), 135.12–142.57-0.482(*ipso*-C), 162.62 (N-HC═O), 165.63(C4 at hydrazine ring).

(E)-4-fluoro-N′-(3-isopropyl-2,6-di(p-methylphenyl)piperidin-4-ylidene) benzohydrazide (Z4)

White powder, yield 75%, mp: 205–207 °C; **IR ranges** (KBr, Vmax Cm^{-1}): 1649(C═O), 1510(C═N), 3280(N-H ring), 3132(NH amide). **H^1 spectra** (400.00 MHz, $CdCl_3$-d6, δ): 0.851, 1.042(doublet, 6-H, 2*CH_3), 2.289(mutiplet, 1H, C-H at piperidine ring), 2.274(singlet, 1H, N-H at piperidine ring), 2.662(double, 1H, C5, 1Ha), 2.798(triplet, -H, C3, 1Ha), 2.869(double-doublet, 1H, 1H, C5, -1He),4.222(double,1H,C2, 1-Ha),4.249(multiplet,1-H, C6, 1-Ha), 7.256–7.400(mutiplet, Aromatic-H), 10.471(singlet, 1H,N-H amide, N-H). **C^{13} ranges** (400.00 MHz, $CdCl_3$, δ):21.192, 21.421 (2*CH_3), 29.63(C-H at piperidine ring), 36.57(C5), 56.262(C3), 62.870(C2), 127.900–133.957(Aromatic-C), 141.10–143.186(*ipso*-C), 162.41(N-H-C═O), 165.06(C4 at hydrazine ring).

(E)-4-fluoro-N′-(2,6-bis(p-fluorophenyl)-3-isopropylpiperidine-4-ylidene) benzohydrazide (Z5)

White crystals, Heed 83%, mp: 182–185 °C; **IR ranges** (KBr, Vmax Cm^{-1}): 1644(CO), 1524(CN), 3239(NH ring), 3189(N-H amide). **H^1 ranges** (400.00 MHz, $CdCl_3$, δ): 0.843, 0.959(doublet, 6-H, 2*CH_3 at piperidine ring), 2.274(mutiplet, 1-H, C-H at piperidine), 1.723(singlet, 1-H, N-H at piperidine), 2.842(double, 1H, C5, 1-Ha), 2.655(triplet, 1-H, C3, 1-Ha), 4.166(double, 1H, C2, 1-Ha), 7.261–7.413 (Aromatic-H), 10.589(singlet, H, N-H amide). **C^{13} spectra** (400.00 MHz, $CdCl_3$, δ): 21.28, 21.09 (2*CH_3 at piperidine ring), 31.36(C-H at piperidine), 37.53(C5), 56.37(C3), 57.43 (C6), 62.79(C2), 127.87–135.19 (Aromatic-C), 142.19–143.20 (*ipso*-C), 162.33(H-N-C═O), 165.10 (C4 at hydrazine ring).

3. Results and discussions

3.1. Physical explanation of complex (Z1)

In proton NMR ranges, a comprehensive and down-field convenient single peak at 10.545 ppm was evocative of the N-H amide group. One more, wide single signal vibrated at 1.656 was consigned for the N-H P^+ for the piperidine ring. Indication widening is in line with the faster conversion of the N-H P^+ with the flush humidity than the reverberation periodical scale. Three doublets were identified in the area of 2.872 ppm, 4.249 ppm, and 4.743 ppm due to 1Ha (C-5), 1Ha (C-6), and 1He (C-2). One double-doublet is perceived in the region of 2.856 ppm due to 1He (C5). Two triplets were seen in the region 1.132 ppm and 2.712 ppm due to 6H at piperidine ring and C-3 (1Ha) respectively. Multiple signals seemed at 2.261 ppm, 7.260–7.475 ppm due to CH at piperidine ring and Aromatic-H.

In C^{13} Nuclear magnetic resonance (NMR) ranges, two down-field reverberations at 163.40 ppm and 159.09 ppm were given CN (C9), and CO (N-NHCO) carbons correspondingly. The carbons

reverberations perceived around 142.540 ppm and 143.972 ppm were in line for *ipso*-C. Though, at hand, there were four signals nearby 36.821, 57.101, 58.102, and 63.861 ppm, and were appropriately allocated to the C5, C3, C6, and C2 separately. The C^{13} organic swing values of the CH_3 carbons (2*CH_3 piperidine ring) were perceived at 21.156 ppm, and 21.30 ppm. The signals at 166.45 ppm were apportioned to C-4 of the hydrazine loop.

3.2. Anti-oxidant prospective

Five, unlike hydrazone by-products, were synthesized and assessed for their *in vitro* free radical scavenging activity in contradiction to numerous open radicals. Our results afford confirmation that synthesized compounds Z **(1–5)** exhibited a concentration-reliant anti-radical activity. The IC_{50} values (half maximal inhibitory concentration) for free radical scavenging of innumerable primed amalgams **Z (1–5)** are publicized in Table 1. It is acknowledged that a gush in phytochemical action is seen with the replacement of alkyl restraints such as $-CH_3$, CH_2CH_3 to -C_6H_5 rings owing to the electric reverberation outcome of the $-C_6H_5$ ring [12]. The imports of the present study display the existence of -CH_3 crowd replacement at the site third of the piperidin-4-one complexes wields an ample inhibitory result in contradiction of numerous free radicals. Compounds owing electron-confer -CH_3 **(Z4)** and methoxy (OCH_3) **(Z3)** replacements at the p-location of the $-C_6H_5$ ring devoted to the Carbon −2nd and Carbon −6th of the piperdin fraction indicated incomparable free radical scavenging special properties equated to the normal anti-oxidant, an acknowledged anti-oxidant used as a +Ve control. Compounds with electron contributing -CH_3 replacement at the third location of the piperidin-4-one blends open surprising deeds. These consequences indorse reports by former workers on *in vitro* free radical scavenging possessions of carbon-based molecules combining an electron contributing group (-CH_3 and $-OCH_3$) at the p- spot of the $-C_6H_5$ hoop [13–16].

Compounds owning electron-realizing Bromo (**Z5),** Chloro **(Z2)** changeovers at the p- location of the piperidine portion bared admired *in vitro* free radical scavenging possessions in contradiction of various free radicals. These fewer or admired open radical scavenging special possessions of the amalgams with Cl and Br might be owing to the electron exodus and the transmission effect of the group-17 (Halogens). Beneath stated outcomes are in contour with surplus findings [13–16]. The radical scavenging outcomes are dignified in colour from purple to light yellow and scrutiny of the transmittance at 517.0 nm [17]. The scavenging ability of the synthesized compounds Z (1–5) is illustrated graphically in Fig. A.

Table 1
IC_{50} values for radical scavenging action (μg/ml).

Complexes	IC 50 values		
	DPPH	Lipid peroxidation	Metal Chelation
Z1	3.7148	3.4205	3.5917
Z2	3.873	3.755	2.8983
Z3	**1.5492**	**1.5492**	**1.3416**
Z4	**1.8166**	**1.2247**	**0.5477**
Z5	3.0496	2.8983	1.9748
Control	**1.8166**	**1.4491**	**1.2247**

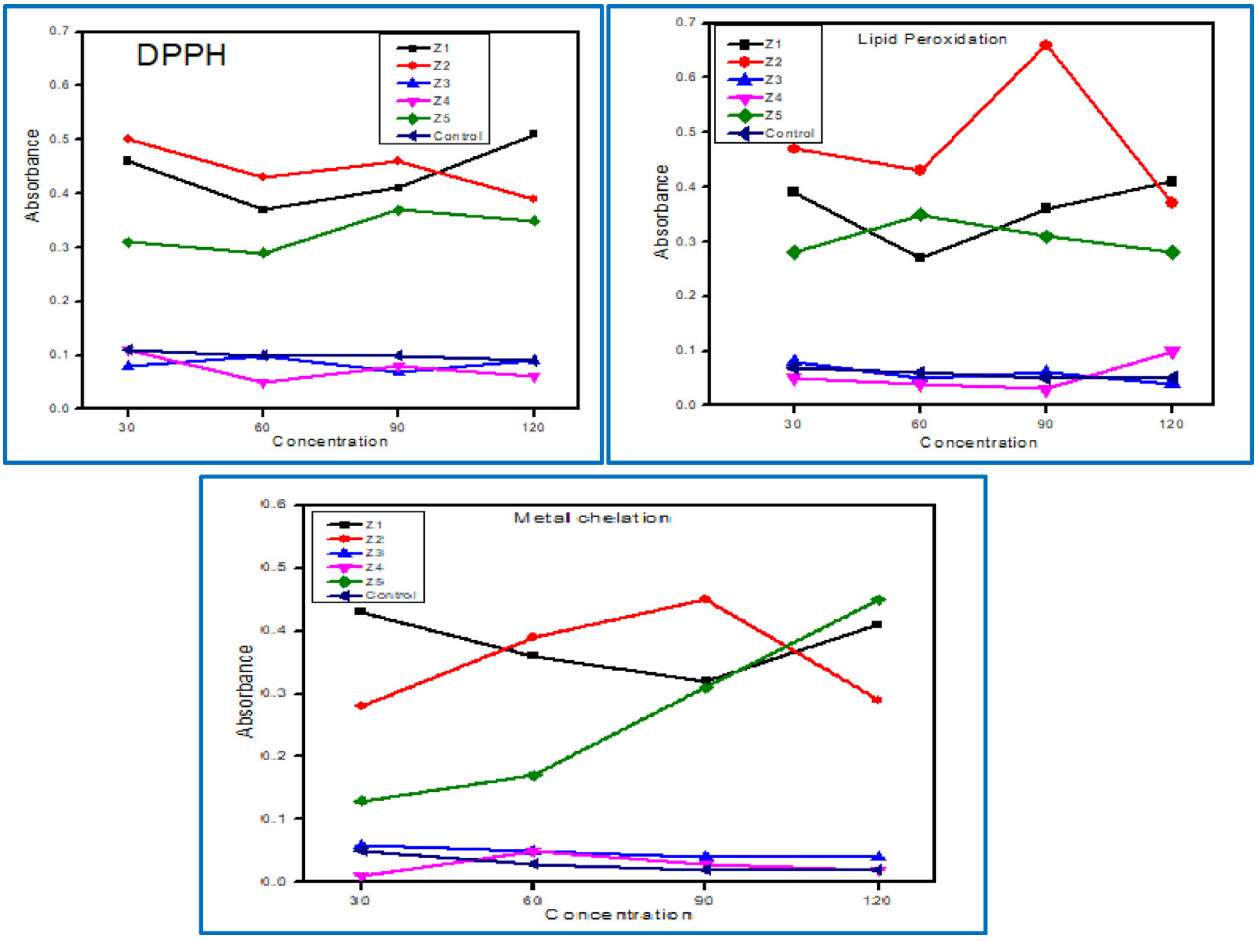


Fig. A. The anti-oxidant potential of synthesized compounds **Z (1–5)**.

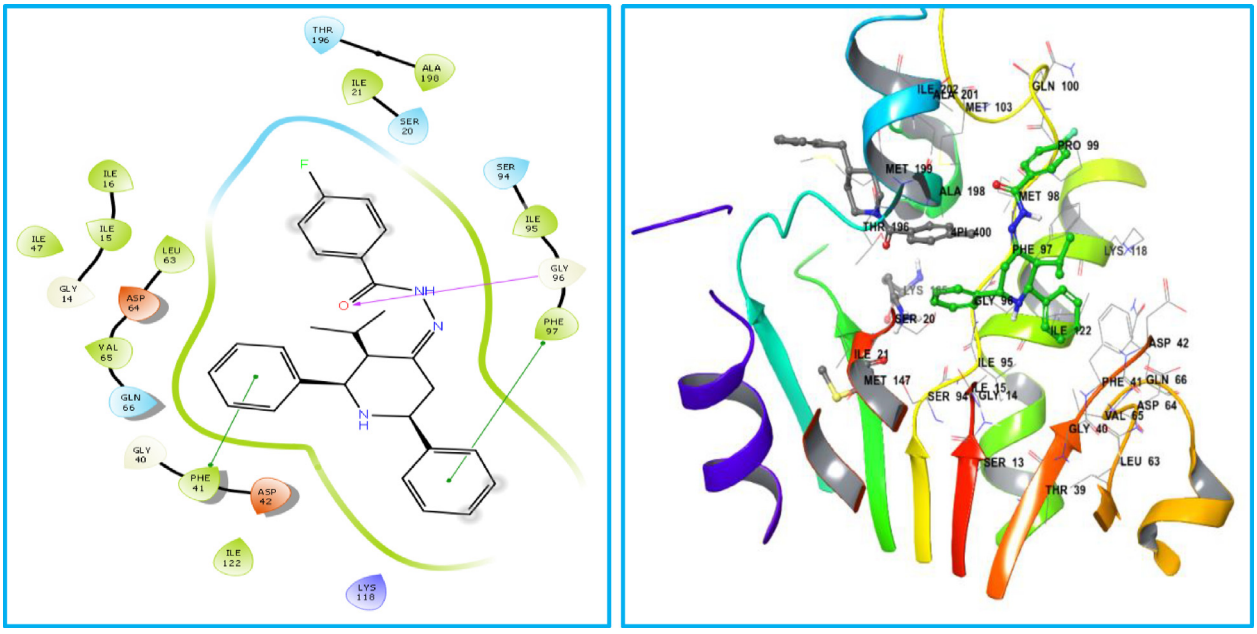


Fig. B. Compound (Z1) docked in the vigorous site of 2NSD and interaction details.

Table 2
Molecular docking (Kcal/mol) outcome of the complex (Z1).

Complex	Glide score	Glide evdw	Glide ecoul	Glide energy	Interacting ruins
Z1	−4.28	−31.78	−4.14	−19.72	H-bond interaction with GLY-96, PHE-41, and PHE-97

3.3. Molecular docking contemplate

To bargain an applicable hindrance for *Tubercle bacillus (TB)* docking contemplates [18,19] were approved for InhA protein. InhA generates the decline of long-chain *trans*-2-enoyl-ACP inside the kind II fatty acid biosynthesis lane of *Tubercle bacillus (TB)* [19]. Hindrance of InhA interrupts the $C_{88}H_{176}O_4$ (mycolic acids) that had remained cherished constituents of the mycobacterial cell wall.

Molecular docking contemplates having been conceded out for the complex **(Z1)**. The docking interface of the complex is presented in Fig. B. The result of the docking study besides the interface vigor is presented in Table 2**.** Scrutiny of the result pageants that the various ions of the complex (**Z1)** show a high glide score value of −4.28 kcal/mol. Therefore, grounded on the docking studies, the complex (Z1) may be suitable to overwhelm the drug confrontation of *Tubercle bacillus (TB)* InhA protein.

4. Conclusion

We bang five new synthesized (E)-4-fluoro-N′-(3-isopropyl-2,6-diphenylpiperidin-4-ylidene) benzohydrazides **Z (1–5)**. All the newly synthesized compounds were screened for their preliminary antioxidant activities. All these compounds display good antioxidant activities might due to the presence of the electron-confer set. The molecular docking study themes out that the complex **Z1** shows a good score value owing to the existence of H-bond interaction. The current studies disclose that these compounds could be an outline for future development in anti-oxidant agents.

CRediT authorship contribution statement

Tanzeer Ahmad Dar: Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft. **Balasankar Thirunavukkarasu:** Conceptualization, Writing – review & editing, Supervision. **A. Ganapathi:** Conceptualization, Writing – review & editing, Supervision. **Winfred Jebaraj:** Conceptualization, Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors are grateful to the Annamalai University, department of chemistry, India for the recording of the NMR spectra, and we are grateful to the Department of Food Science and Technology, University of Kashmir, Srinagar 190006, India for the antioxidant studies.

References

[1] (a) M. Parveen, F. Ahmad, A.M. Malla, S. Azaz, SiO2-H3BO3 promoted solvent-free, Green and sustainable synthesis of bioactive 1-substituted-1H-tetrazole analogues, New J. Chem. 39 (2015) 2028–2041;
(b) M. Parveen, F. Ahmad, A.M. Malla, S. Azaz, M.R. Silva, P.s.p., Silva,[Et3NH][HSO4]-mediated functionalization of hippuric acid: an unprecedented approach to 4-arylidene-2-phenyl-5(4H)-oxazolones, RSC Adv. 5 (2015) 52330–52346;

(c) M. Parveen, A.M. Malla, M. Alam, F. Ahmad, P.S.P. Silva, M.R. Silva, Two new phenolic compounds from Ficus rumphii and their antiproliferative activity, Nat. Prod. Res. 28 (2014) 646–652;
(d) S. Kumar, M. Ceruso, T. Tuccinardi, C.T. Supurans, P.K. Sharma, Pyrazolylbenzo[d] Imidazole as new potent and selective inhibitors of carbonic anhydrase isoforms hCA IX and XII, Bioorg. Med. Chem. 24 (2016) 2907–2913;
(e) M. Parveen, S. Azaz, A.M. Malla, F. Ahmad, M. Ahmad, M. Gupta, SiO2/ZnBr 2 mediated expeditious approach to 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one derivatives in water under microwave irradiation, RSC Adv. 6 (2016) 148–162;
(f) A.M. Malla, M. Parveen, F. Ahmad, S. Azaz, M. Alam, [Et3NH] [HSO4]-catalyzed eco-friendly and expeditious synthesis of thiazolidine and oxazolidine derivatives, RSC Adv. 5 (2015) 19552–19569.

[2] T.D. Montgomery, V.H. Rawal, Palladium-Catalyzed Modular Synthesis of Substituted Piperazines and Related Nitrogen Heterocycles, Org. Lett. 18 (2016) 740–743.

[3] K.C. Nicolaou, J.S. Chen, Total Synthesis of Complex Heterocyclic Natural Products, Pure Appl. Chem. 80 (2008) 727–742.

[4] M.A. Ciufolini, Synthetic Studies on Heterocyclic Natural Products, IIFarmaco 60 (2005) 627–641.

[5] M. Asif, Recent Efforts for the Development of Antitubercular Drug Containing Diazine Ring, Med. Chem. 2 (2012) 151–167.

[6] M. Aldeghi, S. Malhotra, L. David, A. Wing, E. Chan, Two- and Three-Dimensional Rings in Drugs, Chem. Biol. Drug Des. 83 (2014) 450–461.

[7] D.L. Comins, Y. Zhang, X. Zheng, N. Carolina, N. Carolina, Photochemical Reactions of Chiral 2,3-Dihydro-4 (1 H) -Pyridones: Asymmetric Synthesis of Perhydrohistrionicotoxin, Chem. Commun. 4 (1998) 2509–2510.

[8] H. Zhao, W. Zhao, J. Zhu, Y. Jia, C. Yu, An Efficient Synthesis of Aldohexose-Derived Piperidine Nitrones: Precursors of Piperidine Iminosugars, Molecules 18 (2013) 6021–6034.

[9] B.A. Ashwar, A. Gani, I.A. Wani, A. Shah, F.A. Masoodi, D.C. Saxena, Production of resistant starch from rice by dual auto claving retrogradation treatment: in vitro digestibility, thermal and structural characterization, Food Hydrocoll. 56 (2017) 108–117.

[10] A. Shah, F.A. Masoodi, A. Gani, B.A. Ashwar, Effect of γ-irradiation on antioxidant and antiproliferative properties of oat β-glucan, Radiat. Phys. Chem. 117 (2015) 120–127.

[11] C.R. Noller, V. Baliah, J. Am. Chem. Soc. 70 (1948) 3853.

[12] S.Y. Ciftci, N.G. Kelekci, U.S. Goksen, G. Ucar, Hacettepe University J. Faculty Pharm. 31 (2011) 27.

[13] H.M. Ali, A. Abo-Shady, H.A. Sharaf Eldeen, H.A. Soror, W.G. Shousha, O.A. Abdel-Barry, A.M. Saleh, Chem Central J. 7 (2013) 53.

[14] K.N. Mohana, C.B. Pradeep Kumar, ISRN Org. Chem. 620718 (2013).

[15] G. Rajitha, N. Saideepa, P. Praneetha, Indian J. Chem. 50 (2011) 729.

[16] T.A. Dar, B. Thirunavukkarasu, A. Ganapathi, J.W. Jebaraj, Chemical synthesis, spectroscopic analysis, antioxidant, and antimicrobial activities of some hydrazones derived from 4-fluorobenzohydrazide, Mater. Today:. Proc. (2021).

[17] A.A. Khan, A. Gani, F.A. Masoodi, U. Mushtaq, A.S. Naik, Structural, rheological, antioxidant, and Functional properties of β–glucan extracted from edible mushrooms Agaricus bisporus, Pleurotusostreatus and Coprinus attrimentarius, Bioact. Carbohydrates Diet. Fibre 11 (2017) 67–74.

[18] G.F. Zha et al., Bioorg. Med. Chem. Lett. 27 (2017) 3148–3155.

[19] I.B. Ramiss, Tuberculosis 118 (2019) 101853.