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Novel Azo-compound derivatives as Significant Antioxidants: Synthesis, Biological Evaluation, and Molecular Docking Studies

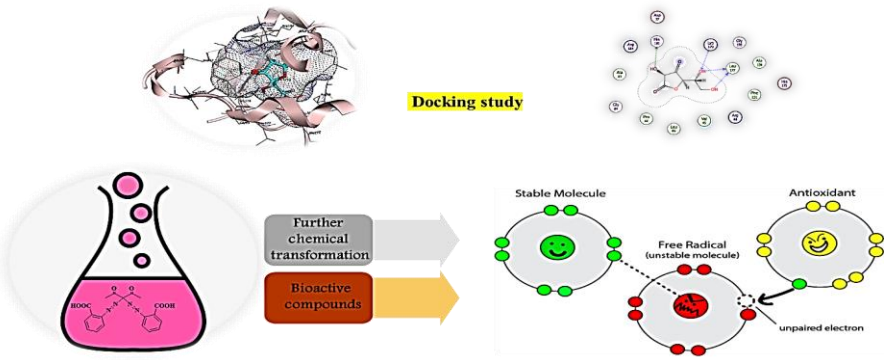
Eman O. Hamed, Doaa A. Elsayed*, Mohamed G. Assy, and Wesam S. Shehab

Department of Chemistry, Faculty of Science, Zagazig University, Zagazig 44519, Egypt;

** Correspondence: doaaatef641995@gmail.com, doaaatef@zu.edu.eg)*

ABASTRACT : ***Due to azo compounds' diverse and intriguing bioactive characteristics, By combining two moles of diazonium salt with one mole of acetylacetone in an alkaline media, it is possible to create azo compounds, such as 2,2'-((2,4-dioxopentane-3,3-diyl) bis(diazene-2,1-diyl) dibenzoic acid. An excellent yield has been achieved in the development and production of several novel diazine and triazine compound derivative products. IR, 1H- NMR, 13C- NMR, and mass spectra were used to examine the composites' structural details. Using the [DPPH] approach, the goods' pharmaceutical activities as antioxidant activity was evaluated. The investigations have amply shown that compound 4 has positive antioxidant effects compared with vitamin C (IC50 = 22.90 µg/mL) as reference. The computational chemistry program MOE (2015) was used to investigate molecular docking for antioxidant activity, using reference substance produced from the cytochrome c peroxidase enzyme, in the database's molecular docking study to investigate the proposed mode of action (PDB code : 2X08, resolution : 2.01).***

GRAPHICAL ABSTRACT



KEYWORDS azo-compound ; antioxidan t; DPPH; Molecular docking.

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I. INTRODICUCTION

Reactive oxygen species (ROS) are a typical byproduct of cellular metabolism in plants. In humans, mitochondrial energy metabolism generates reactive oxygen species (ROS), mostly oxygen ions, as well as related substances peroxides (inorganic and organic). Some of these radicals are necessary for normal cellular processes, such as the transmission of neurological signals **[1]**.

Furthermore, the overproduction of ROS poses a number of threats and dangers to the human body **[2]**. Sufficient (ROS) and (RNS) can harm all biological macromolecules. By degrading the lipid in cell membranes,

ROS can degrade human cells, altering their permeability and leading to DNA cleavage **[3]**. The human body is exposed to a number of dangers from oxidative stress, including diabetes, Alzheimer's **[2]**, neurodegenerative disorders, inflammatory illnesses, ischemia-reperfusion damage, and ageing **[4]**.

Under normal physiological conditions, most chemicals grow at low rates and are cleared by intracellular antioxidant mechanisms such as superoxide dismutase (SOD) and small molecules such as vitamins C and E. **[4]**. However, excessive ROS levels necessitate the use of extremely strong antioxidants to prevent bodily harm.

Numerous fruits and vegetables contain ascorbic acid (vitamin C), which is essential for human nutrition. In 1928, Szent-Györgyi discovered ascorbic acid in the adrenal glands, lemons, cabbages, and oranges as a "acidic carbohydrate," **[5]**. Its chemistry and biology were discovered in the 1990s **[6]**. One of ascorbic acid's most crucial roles in the body is as an antioxidant. It is highly effective at preventing ROS damage to bodily cells **[7]**. It is very effective in removing peroxides and turning them into water **[8]**. Ascorbate has a variety of direct antioxidant actions in vitro that are all extremely efficient **[9].**

Undoubtedly, heterocyclic molecules, especially those with nitrogen, oxygen, and sulphate atoms, have important biological functions **[10]**, **[11]**. In this study, we produced hetero cyclization of azo-compound is considered as a starting step for the generation of new families of compounds that exhibit various pharmaceutical activities as antioxidants **[12, 13]**, especially, the cyclization to produce triazine and diazine derivatives where their structures are desirable in a number of bioactive heterocyclic scaffolds with promising biological action.

We also investigated the synthesized medications using molecular docking, which can predict the most frequent binding mode(s) of a receptor with a protein in a three-dimensional geometry. **[14-16]**. In the present work, a number of azo-compounds were synthetized by using innovated steps. The chemicals were discovered by using IR, ^{1}H- NMR, ^{13}C- NMR and mass spectra in addition to reveling their actual influence as antioxidant. The experimental data were provided by computational studies (molecular docking) by using MOE (2015).

II. EXPERIMENTAL

Materials and methods

High-quality materials were employed to complete this resesrch. Sigma-Aldrich provided all of the chemicals (Taufkirchen, Germany). El-Nasr Pharmaceutical Chemicals Company supplied all solvents (analytical reagent grade, Egypt). The melting points were tested using a Cole-Parmer digital Electrothermal IA 9100 Series equipment (Beacon Road, Stone, Staffordshire, ST15 OSA, UK) are uncorrected. C, H, and N analyses were carried out on a PerkinElmer CHN 2400. The FT-IR 460 PLUS was used to create IR spectra (KBr disks). For generating ^{1}H and ^{13}C-NMR spectra, a Bruker 400, 100 MHz NMR Spectrometer was utilized, the solvent was DMSO-d_6, and chemical shifts were represented in (ppm) in the Main Laboratories of Chemical war, Nasr city, Egypt. Thin-layer chromatography (TLC) sheets coated with UV fluorescent silica gel Merck 60 F254 plates were used to monitor the reactions, which were observed using a UV laser and various solvents as mobile phases. Pharmacognosy Department, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt, tested the biological activity as antioxidant. Molecular docking studies were applied by using MOE software (2015).

synthesis

2,2'-((2,4-dioxopentane-3,3-diyl)bis(diazene-2,1-diyl))dibenzoic acid (2):

To a solution of anthranilic acid (0.274g, 0.002 mol) in (0.2 mL conc. HCl and 3 mL ice distilled water), the solution of $NaNO_2$ (0.138g, 0.002 mL) in (1 mL ice distilled water) added drop by drop then added acetylacetone (0.200g, 0.192mL, 0.001 mol) and solution of sodium acetate (0.1g) in (1 mL ice distilled water). For 1 hour, the reaction mixture was shaken on an ice path. The resulting solid was recovered and recrystallized from ethanol. as a yellow powder of compound **2**: 97%, m.p.: ›300°C. IR (KBr, ν, cm^{-1}): 3444 (broad band for 2 OH), 3051-2839 (CH for aromatic and aliphatic), 1678 (C=O for 2 carboxylic groups), 1624 (C=O for 2 ketones), 1450 (2 N=N). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ = 2.421 (s,6*H*, 2CH_3 of C=O), 7.121- 7.161 (t, 1*H*, *J= 8*, H_{Aryl}), 7.491- 7.533 (t, 1*H*, *J= 8.4*, H_{Aryl}), 7.867- 7.888 (d, 1*H*, *J= 8.4*, H_{Aryl}), 7.955 - 7.974 (d, 1*H*, *J= 7.6*, H_{Aryl}), 15.842 (s, 2*H*, 2OH exchangeable by D_2O). ^{13}C-NMR (DMSO-d_6, 100 MHz): δ = 26.84(2CH_3),

115.04(2Phenyl carbon), 124.07(C), 125.79, 131.04, 131.72, 134.10, 143.82 (2Phenyl carbon), 168.81(2COOH), 194.15, 197.29 (2C=O). MS (*M/Z*): $M^{+\bullet}$ (396.56), Base-peak (207.28). Anal.Calcd. for $C_{19}H_{16}N_4O_6$ (396.36): C,57.58; H, 4.07; N, 14.14; Found; C,57.56; H, 4.06; N, 14.12%.

General procedure for (3, 4):

In the existence of a few drops of triethylamine, a solution of compound 2 (0.792 g, 0.002 mol) in (3.5 mL) dimethylformamide was followed by the addition of thiosemicarbazide & semicarbazide (0.002 mol) in (1.5 mL) distilled water (0.2 mL). The reaction mix was refluxed for 15 hours, then cooled overnight before being dumped over ice cubes and filtered each one by one. The separated solid was recrystallized by a mixture of petroleum ether and ethanol by the ratio (1:1) to produce compounds **3** & **4**.

1-(4-methyl-2-thioxo-1,2-dihydro-4a*H*-benzo[e][1,2,4]triazino[6,1-c][1,2,4]triazin-4a-yl)ethan-1-one (3):

Yellow powder. Yield: 73%, m.p.:188°C. IR (ν, cm^{-1}): 3224 (broad band for NH), 3130 (CH for aromatic), 1677 (C=O), 1574 (C=N), 1395 (N=N), 1263 (C=S). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ = 2.428 (s, 3*H*, CH_3), 2.452 (s, 3*H*, CH_3-C=O), 7.206- 7.247 (t, 1*H*, *J= 8.4*, H_{Aryl}), 7.407 - 7.428 (d, 1*H*, *J= 8.4*, H_{Aryl}), 7.438 - 7.477 (t, 1*H*, *J= 6.8*, H_{Aryl}), 7.557 - 7.576 (d, 1*H*, *J= 7.6*, H_{Aryl}), 13.140 (s,1*H*, NH exchangeable by D_2O). ^{13}C-NMR (DMSO-d_6, 100 MHz): δ = 27.00 (CH_3), 31.63(CH_3), 115.91, 116.69, 117.61, 124.45, 130.64, 131.85, 135.08 (Phenyl carbon), 168.30(C=N), 196.04(C=S), 197.19(C=O). Anal.Calcd. for $C_{12}H_{11}N_5OS$ (273.31): C,52.73; H, 4.06; N, 25.62; S,11.73; Found; C,52.72; H, 4.05; N, 25.60; S, 11.71%.

4a-acetyl-4-methyl-1*H*-benzo[*e*][1,2,4]triazino[6,1-*c*][1,2,4]triazin-2(4a*H*)-one (4):

Yellow powder. Yield: 85%, m.p.:218-220°C. IR (ν, cm^{-1}): 3205 (broad band for NH), 3120 (CH for aromatic), 1692 (C=O of ketone), 1654 (C=O of NH-C=O), 1593 (C=N), 1491 (N=N). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ = 2.433 (s, 3*H*, CH_3), 2.452 (s, 3*H*, CH_3-C=O), 7.408- 7.440 (t, 1*H*, *J= 8.4*, H_{Aryl}), 7.450- 7.469 (d, 1*H*, *J= 7.6*, H_{Aryl}), 7.548- 7.568 (d, 1*H*, *J= 8*, H_{Aryl}), 7.643- 7.681 (t, 1*H*, *J= 7.6*, H_{Aryl}), 13.017 (s,1*H*, NH exchangeable by D_2O). ^{13}C-NMR (DMSO-d_6, 100 MHz): δ= 27.05(CH_3), 31.63(CH_3), 115.96, 116.80, 117.66, 124.50, 130.71, 131.89, 135.20 (Phenyl carbon), 168.30(C=N), 196.04(C=S), 197.19(C=O). Anal.Calcd. for $C_{12}H_{11}N_5O_2$ (257.25): C,56.03; H, 4.31; N, 27.22; Found; C,56.01; H, 4.29; N, 27.21%.

General procedure for (5, 6):

In the presence of a few drops of triethylamine (0.2 mL), a combination of compound 2 (0.792 g, 0.002 mol), thiourea & urea (0.002 mol) was dissolved in (1.8 mL) dimethyl formamide. After 15 hours of thermal reaction, the mixture was chilled before being poured over crushed ice. A solution of petroleum ether (60-80) and collect the residue and recrystallize with ethanol was utilized. **5**&**6**.

1-(3-methyl-1-thioxobenzo[*e*]imidazo[5,1-*c*][1,2,4]triazin-3a(1*H*)-yl)ethan-1-one (5):

Black powder. Yield: 48%, m.p.:198-200°C. IR (ν, cm^{-1}): 2924 (CH for aliphatic), 1672 (C=O), 1581 (C=N), 1486 (N=N), 1265 (C=S). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ = 2.44 (s, 3*H*, CH_3), 2.46 (s, 3*H*, CH_3-C=O), 7.21 - 7.25 (t, 1*H*, *J= 8*, H_{Aryl}), 7.67 - 7.71 (t, 1*H*, *J= 8*, H_{Aryl}), 7.95- 7.97 (d, 1*H*, *J= 8*, H_{Aryl}), 7.99- 8.01 (d, 1*H*, *J= 8*, H_{Aryl}). Anal.Calcd. for $C_{12}H_{10}N_4OS$ (258.30): C,55.80; H, 3.90; N, 21.69; S,12.41; Found; C,55.73; H, 3.86; N, 21.53; S, 12.36%.

3a-acetyl-3-methylbenzo[*e*]imidazo[5,1-*c*][1,2,4]triazin-1(3a*H*)-one (6):

Brownish- yellow powder. Yield: 89%, m.p.:230°C. IR (ν, cm^{-1}): 2918.07 (CH for aliphatic), 1695.60 (C=O of ketone), 1632 (-N-C=O). 1598 (C=N), 1481 (N=N). ^{1}H-NMR (DMSO-d_6, 400 MHz): δ = 2.436 (s, 3*H*, CH_3), 2.455 (s, 3*H*, CH_3-C=O), 7.217- 7.254 (t, 1*H*, *J= 7.2*, H_{Aryl}), 7.668- 7.708 (t, 1*H*, *J= 7.2*, H_{Aryl}), 7.941- 7.965 (d, 1*H*, *J= 9.6*, H_{Aryl}), 7.985- 8.008 (d, 1*H*, *J= 9.2*, H_{Aryl}). ^{13}C-NMR (DMSO-d_6, 100 MHz): δ = 27.31(CH_3), 32.17(CH_3), 116.00(C), 123.95, 124.46, 131.85, 134.95, 135.17, 143.95(Phenyl carbon), 168.13(C=N), 195.88(N-C=O), 197.60(C=O). Anal.Calcd. for $C_{12}H_{10}N_4O_2$ (242.24): C,59.50; H, 4.16; N, 23.13; Found; C,59.48; H, 4.14; N, 23.12%.

Pharmacology

Antioxidant activity screening assay:

The capacity of the matching substances to donate hydrogen atoms or electrons was determined by bleaching the purple color of a methanolic solution of diphenylpicrylhydrazyl (DPPH). The used chemical in this spectrophotometric experiment was the stable free radical diphenylpicrylhydrazyl (DPPH). To produce a final concentration of 1 mg/mL, the tested substances were dissolved in methanol. 0.4 mL of 0.1 *mM* DPPH in methanol was added to 200 mL of each sample. The absorbance was measured against a blank at 517 nm after 30 minutes of incubation in the dark. Standard antioxidants were ascorbic acid (vitamin C). DPPH was not used in the blank sample, and methanol was used instead of the sample. Instead of the tested substance, methanol was used as a negative control sample **[17]**. The following equation was used to compute the radical scavenging activity:

$$1\% = (A_{blank} - A_{sample})/(A_{blank}) \times 100$$

Computational Chemistry

Docking study:

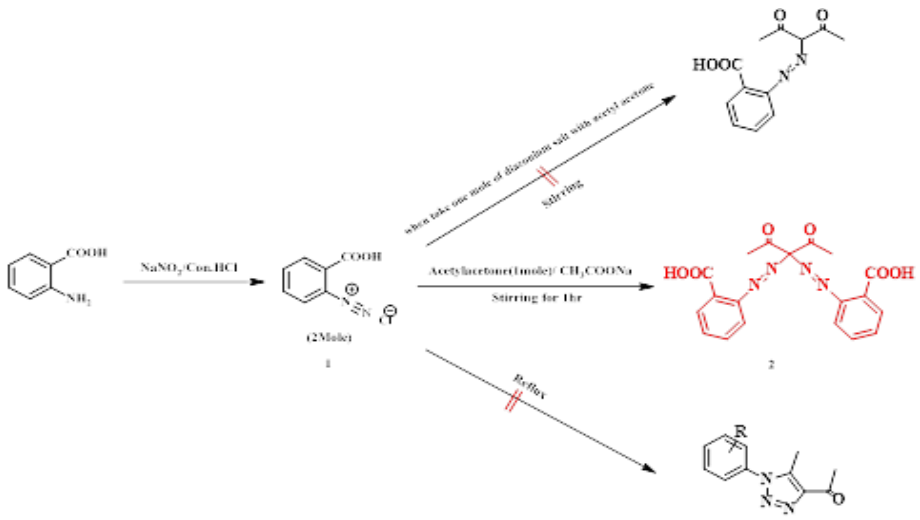
Chemdraw 12.0 was used to create the computational approaches for the most bioactive substances that would be docked using Molecular Operating Environment software (2015). The London DG force and force field energy were used to evaluate the data. All minimizations were completed using MMFF 94 (Merck molecular force field 94) until (RMSD) gradient of 0.1 kcalmol $^{-1}$ A $^{-1}$ was attained **[18, 19]**, and partial charges were estimated automatically. The dock function (S, Kcal/mol) of the MOE programme was used to assess the ligand's binding ability.

The enzyme's X-ray crystal structure in PDB format was acquired from the protein data bank (PDB ID: 2X08, resolution: 2.01) (**https://www.rcsb.org/structure/2X08**). The enzyme was planned for docking investigations by removing water, adding all hydrogen bonds, fixing potential, generating fake atoms from the resultant alpha spheres **[20]**, and then analyzing the ligand interaction with the amino acids in the active site. The largest negative value for the active ligand yields the best Docking Score **[21, 22]**.

III. Results and Discussion

Chemistry

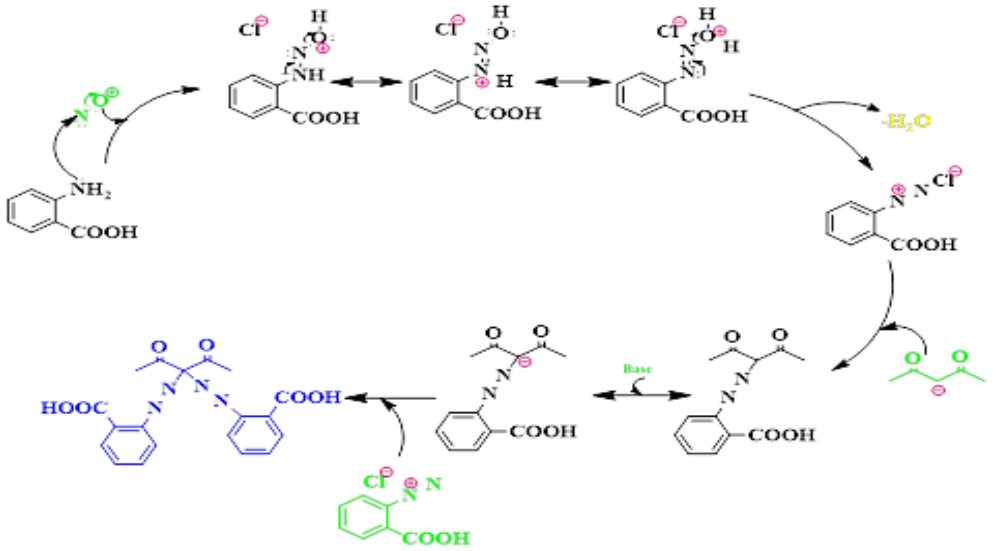
Previous studies showed that, based on the stirring or reflux circumstances, acetylacetone combined with two equal of diazonium salt produced 2-((2,4-dioxopentan-3-yl)diazenyl)benzoic acid or 1-[4-(4-Acetyl-5-methyl-1*H*-1,2,3-triazol-1-yl)-phenyl]ethenone **[23, 24]** . In contrast, two amounts of **1** were combined with acetylacetone in the current technique to produce 2,2'-((2,4-dioxopentane-3,3-diyl)bis(diazene-2,1-diyl))dibenzoic acid **2 (Scheme 1)**.



SCHEME (1) The synthesis of 2,2'-((2,4-dioxopentane-3,3-diyl)bis(diazene-2,1-diyl))dibenzoic acid.

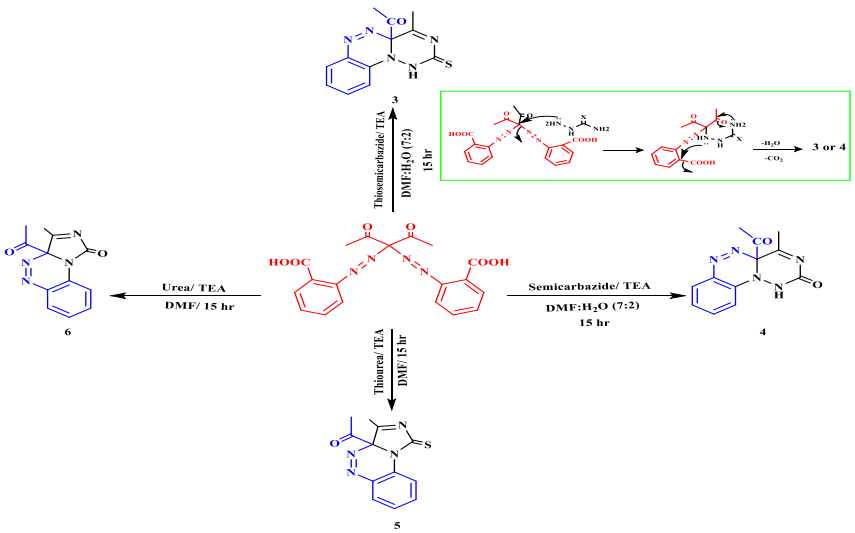
The Infrared spectra of **2** exhibited a broad region between 3444.87 and 3360 cm^{-1}, that related to the OH group in the carboxylic group. Peaks at 1678 cm^{-1}, 1624 cm^{-1}, and 1450 cm^{-1}, respectively, were associated with

the (2C=O for carboxylic group), (2C=O for ketones), and (2N=N), while the ^{1}H-NMR signal decided to show at 15.843 *ppm* for the 2-OH that is exchangeable Carbonyl's carbon was found to be at 197.29 *ppm* in ^{13}C-NMR spectra, whereas acid's carbon was found to be at 168.21 *ppm*. The structural peak was seen on the MS (M/Z) at (396.56), while the base signal was visible at (207.28). The diagram depicts a potential mechanism for the reaction **(Scheme 2).**



SCHEME (2) The conceivable synthesis mechanism of 2,2'-((2,4-dioxopentane-3,3-diyl)bis(diazene-2,1-diyl))dibenzoic acid (2).

The creative stagey of polycyclic substances were produced by attacking quaternary electrophilic carbon with nucleophilic substitution, eliminating the diazonium molecule, proceeded by the azine, and then nucleophilic aromatic substitution, eliminating the formate group, producing the polycyclic result. Therefore, 1-(4-methyl-2-thioxo-4a*H*-benzo[e][1,2,4]triazino[6,1-c] Thiosemicarbazide was used to create [1,2,4]triazin-4a-yl)ethan-1-one **3**; its structure was revealed by the elimination of the hydroxy group in the IR and ^{1}H-NMR spectra, resulting to the observation of a single signal at 13.140 *ppm* for the stretching peak of the -NH group. The structures of the polycyclic formulas **4**, **5**, and **6** were supplied by elemental analysis and spectrum data, as demonstrated in the experimental section, and all three share the same mechanistic route **(Scheme 3).**



SCHEME (3) The synthesis of Benzo triazine and Imidazo triazine derivatives.

Pharmacology

Antioxidant activity screening assay:

The results presented in **table (1)** demonstrated the varying significant levels of free radical scavenging activity where **4›3** with IC_{50} (51.88, 60.05µg/mL), respectively. The synthesized compounds were evaluated as antioxidants utilizing diphenylpicrylhydrazyl. This showed that compound **4** had moderate activity relative to vitamin C (IC_{50} = 22.90 µg/mL).

Table 1: The newly synthesized compounds' antioxidant characteristics.

Comp.	Conc (µM)						
	10	20	40	60	80	100	IC_{50}
Vit. C	31.6	46.2	58.1	70.3	86.4	92.3	22.90±0.12
4	10.8	19.8	34.3	51.7	69.1	82.6	51.88±0.29
3	13.5	21.7	29.8	47.1	62.0	70.3	60.05±0.33

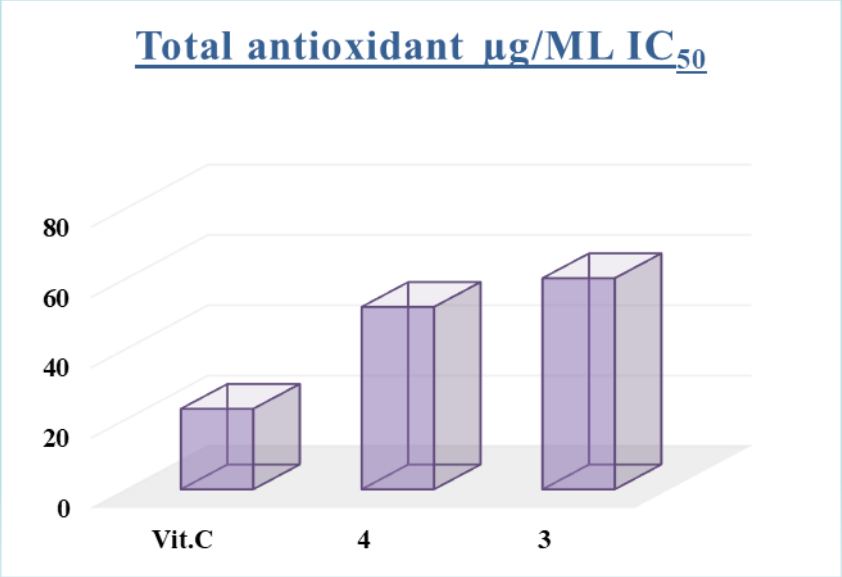


Fig. 1: A statistical depiction of the newly synthesized chemicals' antioxidant activity.

Computational Chemistry

Molecular docking study:

The newly developed and synthesized therapeutic targets were compared to ascorbic acid, a reference substance produced from the cytochrome c peroxidase enzyme, in the database's molecular docking study to investigate the proposed mode of action (PDB code: 2X08). The goal of this research was to gain a better knowledge of how the chemicals created to attach to the cytochrome c peroxidase enzyme's protein-binding site.

To confirm the outcomes of the current docking experiment at the active site, the co-crystallized ligand ascorbic acid was docked into the active site again utilizing the same number of factors. The root mean square deviation (RMSD) and energy score for the best-docked position were both 0.892 and -5.32 Kcal/mol, respectively, supporting the docking study performed with MOE software. Ascorbic acid created four hydrogen connections with His181, Leu177, (two hydrogen bond) and Lys179 **figure 2**.

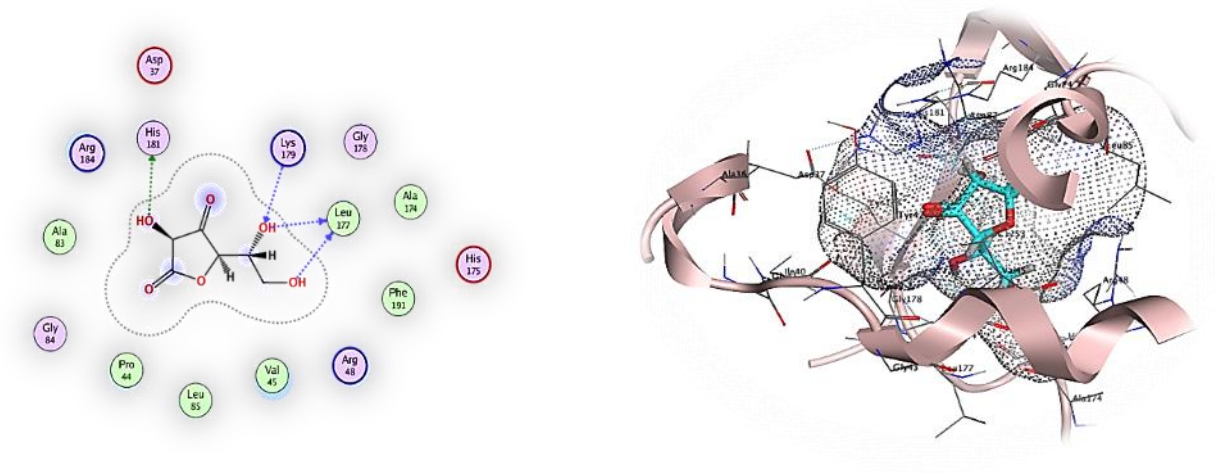
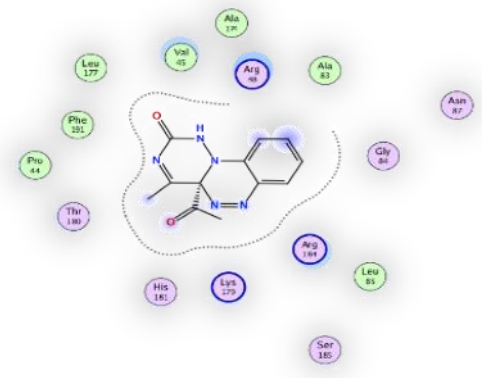
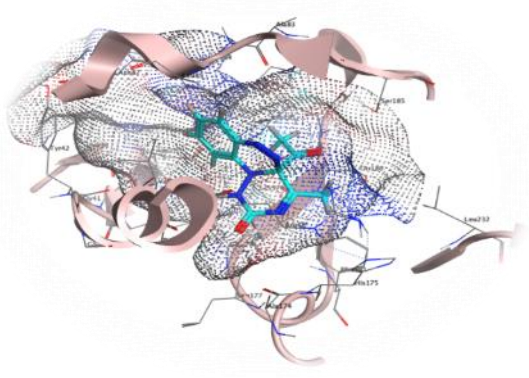


Figure 2. 2D receptor interactions and 3D receptor interactions of reference ascorbic acid.

Compounds **4** suggested binding mode has energy score of -6.8340 kcal/mol. Compound **3** has an energy value of -6.7566 kcal/mol, as shown in **table (2) (figure3)**. The score of these compounds sure that this compound is very stablein the protein-binding site of the cytochrome c peroxidase enzyme.

Table 2. The binding scores, RMSD values, distance and receptor interactions of the most three promising compounds (4 and 3) compared to the docked reference ascorbic acid for antioxidant activity.

Comp.	Score (Kcal/mol)	RMSD	Interacting residues		
			Receptor interactions	Distance (Å)	E (Kcal/mol)
Ascorbic acid	-5.324	0.892	His181/H-donor	3.15	-3.10
			Leu177/H-donor	3.13	-.70
			Leu177/H-donor	3.04	-1.70
			Lys179 H-acceptor	3.15	0.3
4	-6.8340	1.195	-	-	-
3	-6.7566	1.234	-	-	-

Comp.	2D receptor interactions	3D receptor interactions
4		

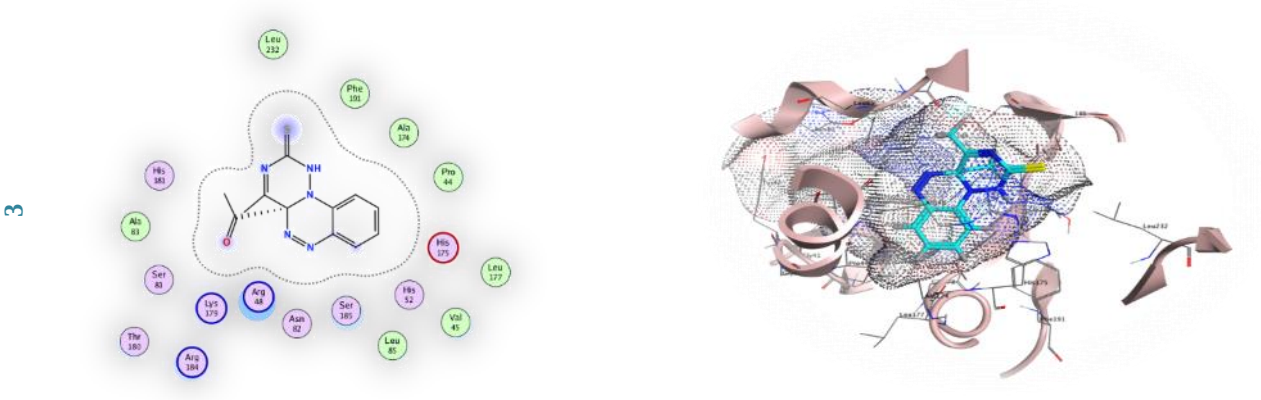


Figure 3. 2D receptor interactions and 3D receptor interactions of synthesized compounds.

VI. CONCLUSION

This work was based on the synthesis of 2,2'-((2,4-dioxopentane-3,3-diyl)bis(diazene-2,1-diyl)dibenzoic acid as azo- compounds which reacted with different reagents to produce the new compounds. These compounds were studied as antioxidant agent through using [DPPH] technique and showed **4›3** with IC_{50} (51.88, 60.05µg/mL), respectively.Finally, the authors designed the molecular docking tentative study which was achieved for the synthesized compounds **3** and **4** with cytochrome c peroxidase enzyme (PDB ID: 2X08, resolution: 2.01). Compounds **4** suggested binding mode has energy score of -6.8340 kcal/mol, while Compound **3** has an energy value of -6.7566 kcal/mol.

DECLARATIONS

Author Contributions: Conceptualization, D.A.E. and W.S.S.; Methodology, D.A.E.; Software, D.A.E.; Validation, D.A.E.; Formal analysis, D.A.E.; Investigation, D.A.E.; Resources, W.S.S. and M.G.A.; Data curation, D.A.E.; Writing—original draft, D.A.E.and E.O.H.; Writing—review & editing, D.A.E., E.O.H., W.S.S. and M.G.A.; Visualization, D.A.E. and W.S.S.; Supervision, M.G.A. and W.S.S.; All authors have read and agreed to the published version of the manuscript.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

V. REFERENCE

[1] **Dayem, A. A., Choi, H.-Y., Kim, J.-H., and Cho, S.-G. (2010):** Role of oxidative stress in stem, cancer, and cancer stem cells. Cancers, 2(2), 859-884.

[2] **Chong, Z. Z., Li, F., and Maiese, K. (2005) :** Stress in the brain: novel cellular mechanisms of injury linked to Alzheimer's disease. Brain Research Reviews, 49(1), 1-21.

[3] **Wang, J. Y., Shum, A. Y., Ho, Y. J., and Wang, J. Y. (2003):** Oxidative neurotoxicity in rat cerebral cortex neurons: synergistic effects of H2O2 and NO on apoptosis involving activation of p38 mitogen-activated protein kinase and caspase-3. Journal of neuroscience research, 72(4), 508-519.

[4] **Maiese, K., Daniela Morhan, S., and Zhong Chong, Z. (2007):** Oxidative stress biology and cell injury during type 1 and type 2 diabetes mellitus. Current neurovascular research, 4(1), 63-71.

[5] **Carpenter, K. J. (2012) :** The discovery of vitamin C. Annals of nutrition and metabolism, 61(3), 259-264.

[6] **Gassmann, B. (1992) :** MB Davies, J. Austin und DA Partridge: Vitamin C: Its Chemistry and Biochemistry. 154 Seiten, 91 Abb., 8 Tab., 10 Originalphotos und 40 Formelgleichungen. The Royal Society of Chemistry, Cambridge 1991. Preis: 13, 50£. In: Wiley Online Library.

[7] **Saffi, J., Sonego, L., Varela, Q. D., and Salvador, M. (2006):** Antioxidant activity of L-ascorbic acid in wild-type and superoxide dismutase deficient strains of Saccharomyces cerevisiae. Redox Report, 11(4), 179-184.

[8] **Zámocký, M., Furtmüller, P. G., and Obinger, C. (2010):** Evolution of structure and function of Class I peroxidases. Archives of Biochemistry and Biophysics, 500(1), 45-57.

[9] **Halliwell, B., and Gutteridge, J. M. (2015):** Free radicals in biology and medicine: Oxford university press, USA.

[10] **AbdEl-Azim, M. H., Aziz, M. A., Mouneir, S. M., EL-Farargy, A. F., and Shehab, W. S. (2020):** Ecofriendly synthesis of pyrano [2, 3-d] pyrimidine derivatives and related heterocycles with anti-inflammatory activities. Archiv der Pharmazie, 353(9), 2000084.

[11] **Shehab, W. S., EL-Farargy, A. F., Abdelhamid, A. O., and Aziz, M. A. (2019):** Synthesis and biological application of pyranopyrimidine derivatives catalyzed by efficient nanoparticles and their nucleoside analogues. Synthetic Communications, 49(24), 3560-3572.

[12] **Reddy, M., Rao, K., Anusha, G., Kumar, G., Damu, A., Reddy, K. R., . . . Reddy, P. V. G. (2021):** In-vitro evaluation of antioxidant and anticholinesterase activities of novel pyridine, quinoxaline and s-triazine derivatives. Environmental Research, 199, 111320.

[13] **Lolak, N., Boga, M., Tuneg, M., Karakoc, G., Akocak, S., and Supuran, C. T. (2020):** Sulphonamides incorporating 1, 3, 5-triazine structural motifs show antioxidant, acetylcholinesterase, butyrylcholinesterase, and tyrosinase inhibitory profile. Journal of enzyme inhibition and medicinal chemistry, 35(1), 424-431.

[14] **Morris, G. M., and Lim-Wilby, M. (2008):** Molecular docking. In Molecular modeling of proteins (pp. 365-382): Springer.

[15] **Kukol, A. (2008):** Molecular modeling of proteins (Vol. 443): Springer.

[16] **Singh, P.; Kumar, R.; Tiwari, S.; Khanna, R.; Tewari, A.; Khanna, H. (2015):** Docking, synthesis and evaluation of antioxidant activity of 2, 4, 5-triaryl imidazole. Clin. Med. Biochem. Open Access, 1, 105.

[17] **Shaaban, S., Negm, A., Sobh, M. A., and Wessjohann, L. A. (2015):** Organoselenocyanates and symmetrical diselenides redox modulators: design, synthesis and biological evaluation. European journal of medicinal chemistry, 97, 190-201.

[18] **Abo Elmaaty, A., Hamed, M. I., Ismail, M. I., B Elkaeed, E., S Abulkhair, H., Khattab, M., and Al-Karmalawy, A. A. J. M. (2021):** Computational insights on the potential of some NSAIDs for treating COVID-19: Priority set and lead optimization. 26(12), 3772.

[19] **Alesawy, M. S., Al-Karmalawy, A. A., Elkaeed, E. B., Alswah, M., Belal, A., Taghour, M. S., and Eissa, I. H. J. A. D. P. (2021):** Design and discovery of new 1, 2, 4-triazolo [4, 3-c] quinazolines as potential DNA intercalators and topoisomerase II inhibitors. 354(3), 2000237.

[20] **Labute, P. J. P. S., Function,, and Bioinformatics. (2009):** Protonate3D: assignment of ionization states and hydrogen coordinates to macromolecular structures. 75(1), 187-205.

[21] **Aziz, M. A., Shehab, W. S., Al-Karmalawy, A. A., El-Farargy, A. F., and Abdellattif, M. H. J. I. j. o. m. s. (2021):** Design, Synthesis, Biological Evaluation, 2D-QSAR Modeling, and Molecular Docking Studies of Novel 1H-3-Indolyl Derivatives as Significant Antioxidants. 22(19), 10396.

[22] **Singh, P., Kumar, R., Tiwari, S., Khanna, R., Tewari, A., and Khanna, H. J. C. M. B. O. A. (2015):** Docking, synthesis and evaluation of antioxidant activity of 2, 4, 5-triaryl imidazole. 1, 105.

[23] **Hamid, A., El-Sayed, H., Mohammed, S., Moustafa, A., and Morsy, H. (2020):** Functionalization of 1, 2, 3-triazole to pyrimidine, pyridine, pyrazole, and isoxazole fluorophores with antimicrobial activity. Russian Journal of General Chemistry, 90(3), 476-482.

[24] **Damade, K. R., Shinde, J. D., Bhojsing, D. J., Patil, V. S., Chauhan, B. S., Kapadane, K. R., and Rajput, C. I. (2018):** Synthesis, Identification and Antibacterial Potency of Azo Dyes having Quinolin-8-ol and Active Methylene Moiety. J. Biol. Chem. Chron, 4(1), 48-54.