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(*E*)-2-[(2,4-dihydroxybenzylidene)amino]benzamide: Synthesis, Antibacterial, Antifungal, Antioxidant and Binding interactions with the 2019-nCoV RBD/ACE2-B0AT1 complex

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Abstract

By simply reacting 2,4-Dihydroxybenzaldehyde (**2,4-DHB**) with 2-Aminobenzamide (**2-AB**), a novel Schiff base (*E*)-2-[(2,4-Dihydroxybenzylidene)amino]benzamide (**2,4-DHBAB**) has been produced. By employing FT-IR, ^{1}H-NMR and ^{13}C-NMR spectrum investigations, the synthesized Schiff base **2,4-DHBAB** was described and its synthesis was validated. By using the well diffusion method and the **DPPH** method, the antibacterial (Gram positive strains of *Staphylococcus aureus*, *Enterococcus sp.*, and Gram-negative strains of *Escherichia coli*, *Klebsiella pneumonia*), antifungal, and antioxidant properties of the Schiff base **2,4-DHBAB** were investigated. The Schiff base **2,4-DHBAB** was showing negative antibacterial and antifungal activities against all the tested pathogens at all the concentrations (25, 50, 100 μL/mL). The Schiff base **2,4-DHBAB** was showing an excellent antioxidant activity (IC_{50}: 55.51) at all five tested concentrations (20, 40, 60, 80, 100 μg/mL) compared to standard drug (Ascorbic acid; IC_{50}: 42.31). The potential binding interactions of Schiff base **2,4-DHBAB** with the 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: **6M17**) was also investigated.

Keywords: Schiff base; Antimicrobial activity; Antioxidant activity; SARS-CoV-2.

1. Introduction

Schiff bases, also known as imines, make them highly valuable in various fields, including medicine, agriculture, and material science. These compounds are formed through the reaction between a primary amine and a carbonyl compound, and their exceptional reactivity and adaptability make them widely used in organic synthesis. In medicine, Schiff bases have shown great potential as drug candidates. Their ability to interact with specific targets in the body makes them valuable in the development of new pharmaceuticals. Additionally, Schiff bases have demonstrated antimicrobial activity, making them effective against various pathogens. In agriculture, Schiff bases have been utilized in the development of novel pesticides and herbicides. [1-15] Their unique chemical structure allows for targeted interactions with pests and weeds, providing effective control while minimizing environmental impact. Furthermore, Schiff bases have found applications in material science. By forming coordination complexes with metal ions, they contribute to the creation of materials with improved conductivity, catalytic activity, and optical properties. Overall, the versatility and reactivity of Schiff bases make them highly sought after for their potential as catalysts, ligands, and antimicrobial agents. Their wide range of applications across different fields highlights their importance in scientific research and development. [16-32]

Salicylaldehyde based Schiff bases are versatile compounds widely used in various fields. These compounds exhibit diverse biological activities, including antimicrobial, anticancer, and antioxidant properties. Their unique chemical structure makes them excellent ligands for metal ions, enabling the development of new coordination complexes. Additionally, Schiff bases derived from salicylaldehyde have shown potential as fluorescent probes and sensors for detecting various analytics. Overall, salicylaldehyde based Schiff bases offer promising applications in medicinal chemistry and materials science. In our previous work, we were synthesized some biologically potential Schiff's bases.[33-38] In this present work, we have been investigated the synthesis of novel Schiff base (*E*)-2-[(2,4-Dihydroxybenzylidene)amino]benzamide (**2,4-DHBAB**) and its antibacterial, antifungal, antioxidant activities and also studied its potential binding modes with the 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: **6M17**).

2. Material and Methods

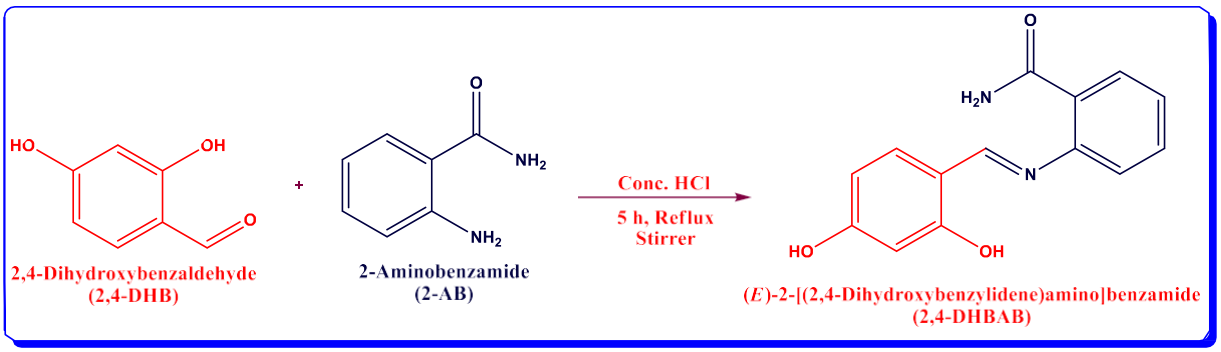
2.1. Materials

2-Aminobenzamide (**2-AB; ≥98%**), 2,4-Dihydroxybenzaldehyde (**2,4-DHB; 98%**), reagents and solvents were purchased from Alfa chemicals. Using KBr pellets, the compounds infrared spectrum had been acquired using a Perkin Elmer FT-IR Spectrophotometer. The ^{1}H-NMR and ^{13}C-NMR spectrrum was analysized by using Bruker Avance III 400 NMR spectrometer in 400 MHz.

2.2. Methods

2.2.1. Synthesis of Schiff base 2,4-DHBAB

The Schiff base (*E*)-2-[(2,4-Dihydroxybenzylidene)amino]benzamide **(2,4-DHBAB)** was synthesized from the simple condensation reaction of 1:1 ratio of 5 mL ethanolic solution of 2,4-Dihydroxybenzaldehyde (**2,4-DHB**) with 5 mL ethanolic solution of 2-Aminobenzamide (**2-AB**) in RB flask. Then 5 mL of Conc. HCl was added to this reaction mixture and followed by refluxed for 5 hours at 60ºC with constant stirred (**Scheme 1**). The obtained yellowish brown solid **2,4-DHBAB** was washed with petroleum ether and then dried well.



Scheme 1. Synthesis of Schiff base 2,4-DHBAB

FT-IR data (υ in cm^{-1}): 3383 (NH), 3189 ($CH_{aromatic\ and\ azomethine}$), 1667 (C=O), 1524 (C=N). ^{1}H NMR data (δ in ppm, d^{6}-DMSO): 10.32 (1H, singlet, **CH=N**), 8.05-8.13, 7.80-7.86, 7.55-7.57, 7.47-7.50, 7.65-7.69, 7.11-7.19, 6.56-6.59, 6.38-6.41 (2H, muliplet, $CONH_2$). ^{13}C NMR data (δ in ppm, d^{6}-DMSO): 171.46 (NH_2-C=O), 154.58 (CH=N), 163.05, 163.12, 162.01, 148.82, 103.83.

2.2.2. Antibacterial and antifungal activity technique (Well diffusion method)

Antibacterial and Antifungal activity were screened the compounds against bacterial pathogens, such as *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus sp*, *Klebsiella*

pneumonia and fungal strain, *Candida albicans* by well diffusion method.[33-38] Using well puncture, 5 mm diameter wells were created on Muller-Hinton agar (**MHA**) and Sabouraud dextrose agar (**SDA**) plates. With sterile cotton swabs, each strain was uniformly swabbed onto the separate plates. The various concentrations of each compound **2,4-DHBAB** (25, 50, and 100µg/mL) were pipetted into each well on each plate using a sterile micropipette. About 50µg/mL of *Nalidixic acid*, *Chloramphenicol* and *Fluconozole* were used as control antibiotics for bacterial and fungal pathogens. For 24 hours, all of the plates were incubated at 37°C. Following incubation, Chemkovil, SIDCO, Salem, Tamilnadu, India, provided help for measuring the zone of inhibition.

2.2.3. Antioxidant activity technique (DPPH method)

The antioxidant activity of **2,4-DHBAB** was evaluated using, with minor adjustments, the method outlined by Afsar *et al.* for the scavenging activity of the stable 1,1-Diphenyl-2-picrylhyorazyl (**DPPH**) free radical. [39,40] A solution of 1 mM **DPPH** in methanol (0.5 mL) was combined with a chemical solution (20, 40, 60, 80, and 100 µg/mL) in 2 mL of methanol. As a reference standard, L-ascorbic acid (20–100 µg/mL) was made along with corresponding blank samples. The control was a mixer with 2 ml of methanol and 0.5 mL of **DPPH** solution. Using a UV-Vis spectrophotometer, the reaction was conducted and the absorbance drop was determined at 517 nm after 30 minutes in the dark. The following formula was used.

$$\textbf{Inhibition \%} = [(A_c - A_s)/A_c] \times 100$$

Where,

A_c is the absorbance of the control

A_s is the absorbance of the sample

2.2.4. Docking method

The 2019-nCoV RBD/ACE2-B0AT1 complex's 3D structure (PDB code: **6M17**, **Figure 1**) was taken from the RCSB Protein Data Bank (Research Collaboratory for Structural Bioinformatics).[41] Discovery Studio is used to visualize the molecular docking poses. To execute molecular docking, the Auto-Dock Tool (1.5.6) was utilized. The procedure and data interpretation were The 3D structure of Schiff base **2,4-DHBAB** was optimized using Gaussian 09W. [39, 40, 42, 43]

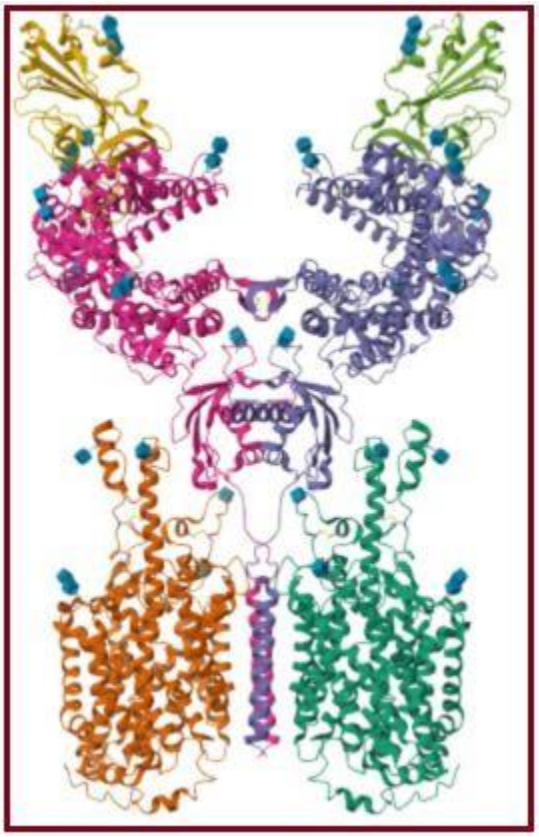


Figure 1. 3D structure of the 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: 6M17)

3. Results and Discussions

3.1. Spectral studies

The FT-IR vibrational stretching mode of Schiff base **2,4-DHBAB** is showed at 3383 cm^{-1}, which is attributed to –NH stretching of amide ($CONH_2$) group of **2,4-DHB** moiety. The aromatic and azomethine -CH stretching peak are showed at 3189 cm^{-1}. The peak at 1667 cm^{-1}, which is assigned to carbonyl (C=O) stretching mode of the amide ($CONH_2$) group of **2,4-DHB** moiety. The C=N bands were observed in the lower frequency at 1524 cm^{-1}, it is clearly indicating the formation of the azomethine nitrogen. The ^{1}H NMR spectrum of Schiff base **2,4-DHBAB** showed two singlet peaks at 3.87 ppm and 3.66 ppm, which are attributed to the phenolic –OH groups in the **2,4-DHB** moiety. The aromatic amide protons showed multiplet peak at 6.38-6.41 ppm. The characteristic peak at 10.32 ppm as singlet, which is assigned to azomethine (**CH=N**) group and it is clearly indicated to the formation of Schiff base **2,4-DHBAB**. The aromatic protons of the **2-AB** moiety showed multiplet peaks at 8.05-8.13 ppm, 7.80-7.86 ppm, 7.55-7.57 ppm and 7.47-7.50 ppm. The peaks are showed at 7.65-7.69 ppm, 7.11-7.19 ppm and 6.56-6.59 ppm, which are assigned to the aromatic protons of the **2,4-DHB** moiety. The ^{13}C NMR spectrum of Schiff base **2,4-DHBAB** showed peak at

171.46 ppm, which is assigned to carbonyl (NH_2-C=O) of amide group in **2-AB** moiety. The peak at 154.58 ppm is assigned to azomethine (CH=N) group. The two phenolic carbons are showed peaks at 163.05, 163.12 ppm and 162.01 ppm. The aromatic carbons of **2,4-DHBAB** and **2-AB** are showed peaks at 103.83-148.82 ppm.

3.2. Biology

3.2.1. Antibacterial activity of 2,4-DHBAB

Antibacterial activity of **2,4-DHBAB** was screened against two gram positive bacterial pathogens, such as *Staphylococcus aureus* and *Enterococcus sp* and two gram negative bacterial pathogens, such as *Escherichia coli* and *Klebsiella pneumonia* by using well diffusion method and their results were summarized in **Table 1**. The *Nalidixic acid* was used as standard drug for gram positive bacterial pathogens and *Chloramphenicol* was used as standard drug for gram negative bacterial pathogens. From its results, the synthesized compound **2,4-DHBAB** as well as standard drugs (*Nalidixic acid* and *Chloramphenicol*) was showed no antibacterial activity against all the tested gram positive and gram negative bacterial pathogens in all tested concentrations (25, 50 & 100μL/mL, **Table 1**).

Table 1. Antibacterial activity of 2,4-DHBAB

Type of bacteria/ Standard drug	**Bacteria for Test**	**Concentration (μL/mL)**	**Zone of inhibitions (mm)**
Gram positive	*Staphylococcus aureus*	25	*NA*[a]
		50	*NA*[a]
		100	*NA*[a]
	Enterococcus sp	25	*NA*[a]
		50	*NA*[a]
		100	*NA*[a]
Standard drug	*Nalidixic acid*	50	*NA*[a]
Gram negative	*Escherichia coli*	25	*NA*[a]
		50	*NA*[a]

		100	*NA*[a]
	Klebsiella pneumoniae	25	*NA*[a]
		50	*NA*[a]
		100	*NA*[a]
Standard drug	*Chloramphenicol*	50	*NA*[a]

[a]*No activity*

3.2.2. Antifungal activity of 2,4-DHBAB

Antifungal activity of **2,4-DHBAB** was screened against one fungal pathogen, such as *Candida albicans* by using well diffusion method and its results were summarized in **Table 2**. The *Fluconozole* was used as standard drug. From their results, the synthesized compound **2,4-DHBAB** was showed no antifungal activity against the tested fungal pathogen in two tested concentrations (25 & 50 µL/mL, **Table 2 & Figure 2**). The zone inhibition of the standard drug *Fluconozole* was showed 15 mm and 22 mm in the concentration of 25 and 50 µL/mL respectively (**Table 2 & Figure 2**). The synthesized **2,4-DHBAB** was showed 8 mm zone inhibition in the concentration of 100 µL/mL and it is showed as moderate antifungal activity compared to the standard drug (28 mm, **Table 2 & Figure 2**).

Table 2. Antifungal activity of 2,4-DHBAB

Compound / Standard drug	***Candida albicans***		
	Zone inhibitions (mm)		
	25	**50**	**100**
2,4-DHBAB[b]	*NA*[c]	*NA*[c]	8
Fluconozole[b]	15	22	28

[b]µL/mL; [c]*No activity*

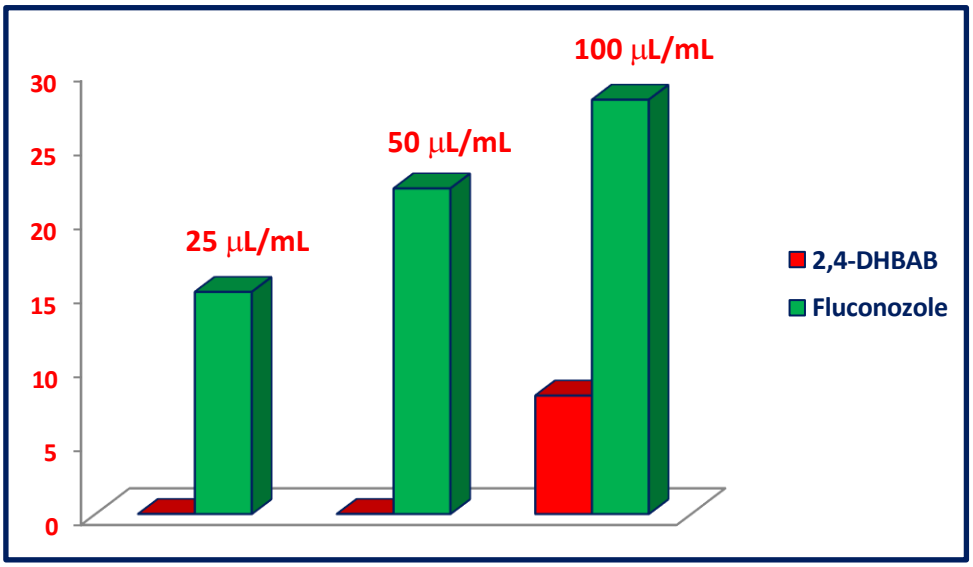


Figure 2. Antifungal activity of 2,4-DHBAB

3.2.3. Antioxidant activity of 2,4-DHBAB

The antioxidant activity of the synthesized compound **2,4-DHBAB** was evaluated on the basis of the scavenging activity of the stable 1,1-Diphenyl-2-picrylhyorazyl (**DPPH**) free radical method and its results was summarized in **Table 3**. The ascorbic acid has been used as a standard drug. The compound **2,4-DHBAB** showed an excellent antioxidant activity (IC_{50}: 55.51) in all the tested concentrations (20, 40, 60, 80 and 100 µg/mL) compared to the standard drug (IC_{50}: 42.31, **Table 3 & Figure 3**). For the concentration of 20 µg/mL, the compound **2,4-DHBAB** showed 19.23% antioxidant activity and it is closed to the standard drug (25.64). The compound **2,4-DHBAB** showed 42.23% antioxidant activity in the concentration of 40 µg/mL, 57.69% antioxidant activity in the concentration of 60 µg/mL, 66.66% antioxidant activity in the concentration of 80 µg/mL and 80.71% antioxidant activity in the concentration of 100 µg/mL (**Table 3 & Figure 3**). The standard drug *Ascorbic acid* showed 51.28%, 70.51%, 82.20% and 98.90% antioxidant activity in the concentration of 40, 60, 80 and 100 µg/mL (**Table 3 & Figure 3**) respectively. The antioxidant activity of the compound **2,4-DHBAB** is very closed to the standard drug (**Table 3 & Figure 3**).

Table 3. Anti-oxidant activity of 2,4-DHBAB

Compound / Standard drug	**Percentage of Inhibition(%, µg/mL)**					**IC_{50}**
	20	**40**	**60**	**80**	**100**	

2,4-DHBAB[b]	19.23	42.23	57.69	66.66	80.71	55.51
Ascorbic acid[b]	25.64	51.28	70.51	82.2	98.9	42.31

[b]µL/mL

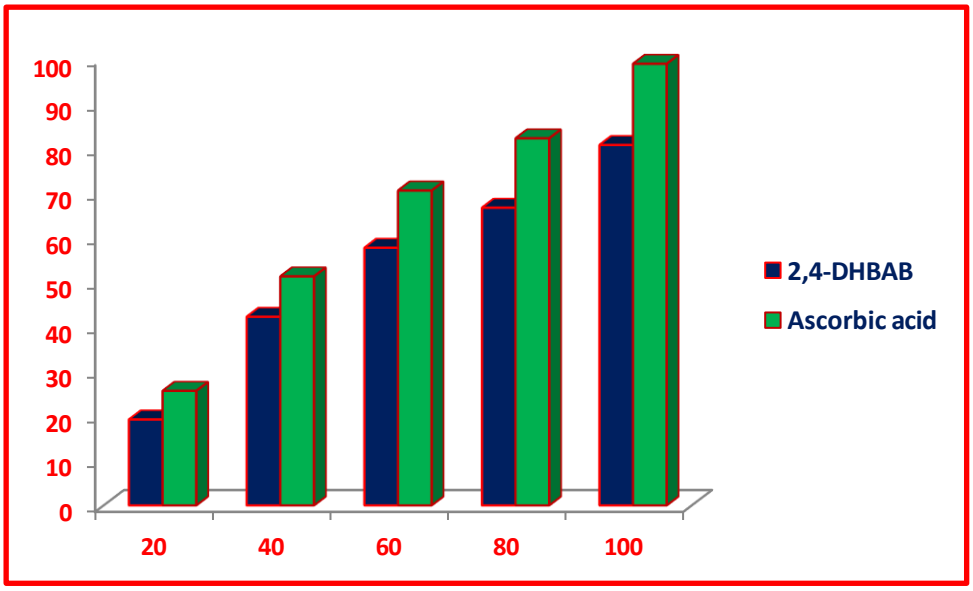


Figure 3. Antioxidant activity of 2,4-DHBAB

3.2.4. Docking study of 2,4-DHBAB

The compound **2,4-DHBAB** was showed better binding potential with the targeted 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: **6M17**, **Figure 4 & Table 4**). The compound showed binding energy as -6.15 kcal/mol and inhibition constant is 31.31 µM (**Table 4**).

Table 4. Binding potential of 2,4-DHBAB with the targeted 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: 6M17)

Compound	Binding energy (kcal/mol)	Inhibition constant (µM)	No of hydrogen bonding	Hydrogen bonding amino acid residue
2,4-DHBAB	-6.15	31.31	---	---

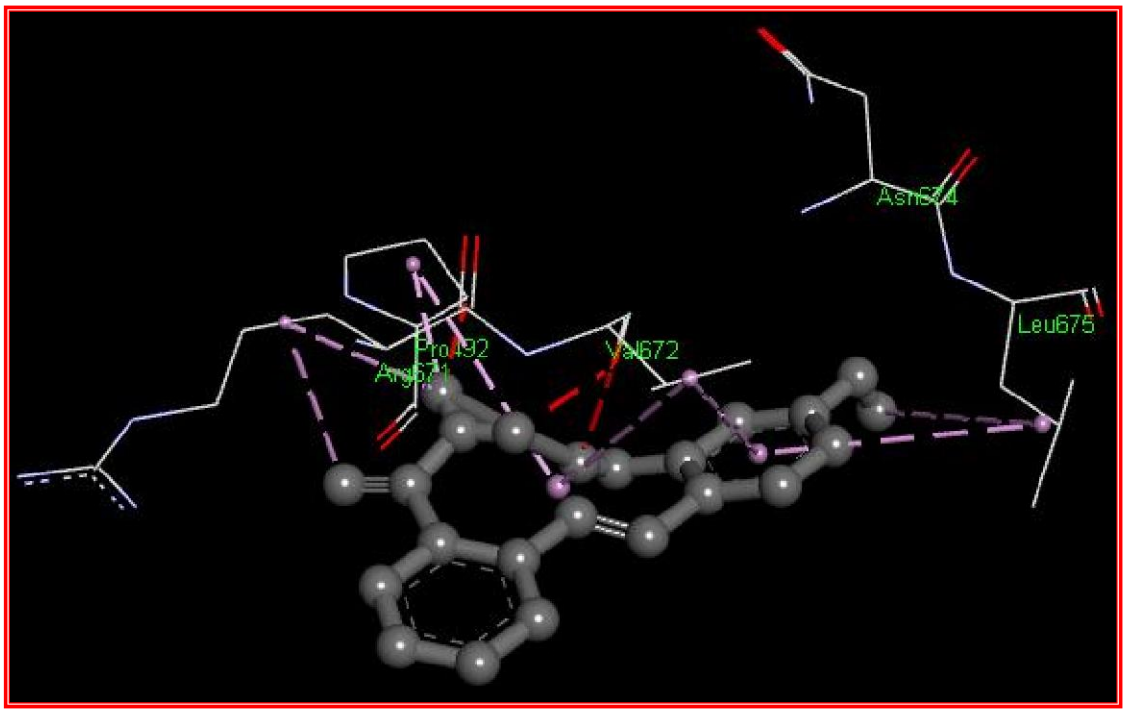


Figure 4. Binding mode and site of 2,4-DHBAB with the targeted 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: 6M17)

4. Conclusions

In conclusion, we have been synthesized a novel Schiff base (*E*)-2-[(2,4-Dihydroxybenzylidene)amino]benzamide (**2,4-DHBAB**) was synthesized by the simple condensation reaction and its structure confirmed by using spectral studies (FT-IR and NMR Spectroscopy). The synthesized compound **2,4-DHBAB** showed undesirable results against all the tested bacterial pathogens in all the concentrations. It should be modified as antibacterial agent in our future. The compound **2,4-DHBAB** showed moderate antifungal activity and an excellent antioxidant activity compared to its corresponding standard drugs. The binding energy and inhibition constant is clearly indicated its potential binding capable with the targeted 2019-nCoV RBD/ACE2-B0AT1 complex (PDB code: **6M17**). However, further research is necessary to examine the potential applications and clinical trial of this compound to inhibit viral infections, and they will be addressed eventually.

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References

[1] Ibrahim AR. Preparation and characterization of some transition metal complexes of bis schiff base ligand. International Journal of Advanced Research. 2015, 3(8):315-324.

[2] Sadia M, Khan J, Naz R, Zahoor M, Shah SWA, Ullah R, et al. Schiff base ligand L synthesis and its evaluation as anticancer and antidepressant agent. Journal of King Saud University. 2020, 33:101331. doi, 10.1016/j.jksus.2020.101331.

[3] Xavier A, Srividhya N. Synthesis and study of schiff base ligands. Journal of Applied Chemistry. 2014, 7(11):06- 15. GSC Biological and Pharmaceutical Sciences, 2022, 21(03), 203–215 214.

[4] Ashraj MA, Mahmood K, Wajid A. Synthesis, characterization and biological activity of schiff base. International Proceedings of Chemical, Biological and Environmental Engineering. 2011, 10:1-7.

[5] Kandile NG, Mohamed MI, Ismaeel HM. Synthesis of new Schiff bases bearing 1, 2,4-triazole, thiazolidine and chloroazetidine moieties and their pharmacological evaluation. Journal of Enzyme Inhibition and Medicinal Chemistry. 2017, 32(1):119-129. doi: 10.1080/14756366.2016.1238365

[6] Suyambulingam JK, Karvembu R, Bhuvanesh NSP, Enoch IVMV, Selvakumar PM, Premnath D, et al. Synthesis, structure, biological/chemosensor evaluation and molecular docking studies of aminobenzothiazole schiff bases. Journal of Adhesion Science and Technology. 2020, 34(23):1-23. doi: 10.1080/01694243.2020.1775032.

[7] Durgun M, Turkes C, Isik M, Demir Y, Sakli A, Kuru A, et al. Synthesis, characterization, biological evaluation and insilico studies of sulphonamides schiff bases. Journal of Enzyme Inhibition and Medicinal Chemistry. 2020, 35(1):950-962. doi: 10.1080/14756366.2020.1746784.

[8] Mermer A, Demirbas N, Uslu H, Demirbas A, Ceylan S, Sirin Y. Synthesis of novel schiff bases using green chemistry techniques, antimicrobial, antioxidant, antiurease activity screening and molecular docking studies. Journal of Molecular Structure. 2019, 1181:412-422. doi: 10.1016/j.molstruc.2018.12.114.

[9] Tehrani KHME, Hashemi M, Hassa M, Kobarfard F, Mohebbi S. Synthesis and antibacterial activity of schiff bases of 5-substituted isatins. Chinese Chemical Letters. 2015, 27(2):221-25. doi: 10.1016/j.cclet.2015.10027.

[10] Manjunath M, Kulkarni AD, Bagihalli GB, Malladi S, Patil SA. Bio-important antipyrine derived schiff bases and theie transition metal complexes: synthesis, spectroscopic characterization, antimicrobial, antihelmenthic and DNA cleavage investigation. Journal of Molecular Structure. 2016, 1127:314-21. doi: 10.1016/j.molstruc.2016.07.123.

[11] Al-Labban HMY, Sadiq HM, Aljanaby AAJ. Synthesis, characterization and study of biological activity of some schiff bases derivatives from 4-amino antipyrine as a starting material. Journal of Physics: Conference Series. 2019, 1294:052007. doi: 10.1088/1742-6596/1294/5/052007.

[12] Mishra VR, Ghanavatkar CW, Mali SN, Chaudhari HK, Sekar N. Schiff base clubbed benzothiazole: synthesis, potent antimicrobial and MCF-7 anticancer activity, DNA cleavage and computational studies. Journal of Biomolecular Structure and Dynamics. 2019, 38(6):1772-85. doi: 10.1080/07391102.2019.1621213.

[13] Teran R, Guevara R, Mora J, Dobronski L, Barrerio-Costa O, Beske T, et al. Characterization of antimicrobial, antioxidant, and leishmanicidal activities of shciff base derivatives of 4-amino antipyrine. Molecules. 2019, 24:2696. doi: 10.3390/molecules24152696.

[14] Singh BB, Shakil NA, Kumar J, Ran VS, Mishra A. Microwave synthesis, characterization and bio-efficacy of novel halogenated schiff bases. Journal of Environmental Science and Health. 2016, 51(8):558-70. doi: 10.1080/03601234.2016.1170558.

[15] Kizilkaya H, Dag B, Aral T, Genc N, Erenle R. Synthesis, characterization and antioxidant activity of heterocyclic schiff bases. Journal of the Chinese Chemical Society. 2020, 67(9):1696-701. doi: 10.1002/jccs.202000161.

[16] Erturk AG. Synthesis, structural identifications of bioactive two novel schiff bases. Journal of Molecular Structure. 2019, 1202:127299. doi: 10.1016/j.molstruc.2019.127299.

[17] Dowling A, Dwyer JO and Adley CC. Antibiotics: Mode of action and mechanism of resistance. 2017, 536-545.

[18] Xu Y, Shi Y, Lei F, Dai L. A novel and green cellulose-based Schiff base-Cu (II) complex and its excellent antibacterial activity. Carbohydrate Polymers. 2020, 230:115671. doi: 10.1016/j.carbpol.2019.115671.

[19] Mahmood WH, Deghadi RM, Mohamed GH. Novel schiff base ligand and its metal complexes with some transition elements. Synthesis, spectroscopic, thermal analysis, antimicrobial and invitro anticancer activity. Applied Organometallic Chemistry. 2016, 30:221-230. doi: 10.1002/aoc.3420.

[20] Hussain Z, Fadhil Z, Adil H, Khalaf M, Abdulah B, Yousif E. Schiff bases containing sulfamethoxazole nucleus. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2016, 7(3):1500-1510. [21] Hassan AS, Awad HM, Magd-EI-Din AA, Hafez TS. Synthesis and in-vitro antitumour evaluation of novel schiff bases. Medicinal Chemistry Research. 2018, 27:915-27. doi: 10.1007/s00044-017-2113-5. [22] Hassan AS, Moustafa GO, Askar AA, Naglah AM, Al-Omar MA. Synthesis and antibacterial evaluation of fused pyrazoles and schiff bases. Synthetic Communications. 2018, 48(21):2761-2772. doi: 10.1080/00397911.2018.1524492. GSC Biological and Pharmaceutical Sciences, 2022, 21(03), 203–215 215.

[23] Ragi K, Kakkassery JT, Raphael VP, Johnson R, Vidhya TK. In-vitro antibacterial and in-silico docking studies of two schiff bases on staphylococcus aureus and its target proteins. Future Journal of Pharmaceutical Sciences. 2021, 7(78). doi: 10.1186/s43094-021-00225-3.

[24] Sakthivel A, Jeyasubramaniyan K, Thangagiri B, Raja JD. Recent advances in schiff bases metal complexes derived from 4-aminoantipyrine derivatives and their potential applications. Journal of Molecular Structure. 2020, 1222:128885. doi: 10.1016/j.molstruc.2020.128885.

[25] Rawat A, Reddy AVB. Recent advances on anticancer activity of coumarin derivatives. European Journal of Medicinal Chemistry Reports. 2022, 5:100038. doi: 10.1016/j.ejmcr.2022.100038.

[26] Liu J, Bu W, Pan L, Shi J. NIR-Triggered Anticancer Drug Delivery by Upconverting Nanoparticles with Integrated Azobenzene-Modified Mesoporous Silica. Angewandte Chemie. 2013, 52:4375-4379. doi: 10.1002/anie.201300183.

[27] Kumar M, Padmini T, Ponnuvel K. Synthesis, characterization and antioxidant activities of schiff bases are of cholesterol. Journal of Saudi Chemical Society. 2014, 21:322-328. doi, 10.1016/j.jscs.2014.03.006.

[28] Iacopetta D, Lappano R, Mariconda A, Ceramella J, Sinicropi MS, Saturnino C, et al. Newly synthesized iminoderivatives analogs of resveratrol exert inhibitory effects in breast tumour cells. International Journal of Molecular Sciences. 2020, 21:7797. doi: 10.3390/ijms21207797.

[29] Amorim CA, Pavani TFA, Lopes AFS, Duque MD, Mengarda ACA, Silva MP, et al. Schiff bases of 4-phenyl-2-amino thiazoles as hits to new antischitosomals: synthesis, in-vitro, in-vivo and in-silico studies. European Journal of Pharmaceutical Sciences. 2020, 150:105371. doi: 10.1016/j.ejps.2020.105371.

[30] Asfandiyarova NS, Philippov EV. The use of nonsteroidal anti - inflammatory drugs in polymorbid pathology. Terapevticheskii arkhiv. 2020, 92(1):82-88. doi: 10.26442/00403660.2020.01.000480.

[31] Raza R, Saeed A, Arif M, Mahmood S, Muddassar M, Raza A, Iqbal J. Synthesis and Biological Evaluation of 3- thiazolocoumarinyl Schiff-base Derivatives as Cholinesterase Inhibitors. Chemistry Biology and Drug Design. 2012, 80:605-615. doi: 10.1111/j.1747-0285.2012.01435.x.

[32] Adebayo JO, Tijjani H, Adegunloye AP, Ishola AA, Balogun EA, Malomo SO. Enhancing the antimalarial activity of artesunate. Parasitology Research. 2020, 119:2749-64. doi: 10.1007/s00436-020-06786-1.

[33] D. Satheesh, A. Rajendran, K. Chithra, R. Saravanan, Chemical Data Collections, 28, 100406 (2020). https://doi.org/10.1016/j.cdc.2020.100406.

[34] Singaram Kannan, Ayyanan Gomathi, Kasi Chithra†, Dhurairaj Satheesh, Binuclear Copper (II) Complexes of Salphen-Type Tetra-Imine Schiff's Bases Derived from 3,3'-Diaminobenzidine with 3-Allylsalicylaldehyde and 3-Ethoxysalicylaldehyde: Synthesis, Characterization and their Antimicrobial Activity. Infokara Research, 9(10) (2020), 236-254.

[35] S. Kannan, A. Gomathi, K. Chithra, D. Satheesh, Synthesis, Characterization, Antibacterial and antifungal activity of Cu(II) homodinuclear complexes of tetra-imine Schiff's base ligands derived from 3,3'-Diaminobenzidine with 3-Hydroxysalicylaldehyde

and 3-Methoxysalicylaldehyde, Infokara Research, 9(10) (2020), 106-131. DOI:16.10089.IR.2020.V9I10.285311.3871

[36] D. Satheesh, K. Jayanthi, Int. J. Chem. and Pharm. Anal., 4, 1179 (2017). http://dx.doi.org/10.21276/ijcpa

[37]. K. Jayanthi, D. Satheesh, World J. Pharm. Res. 6, 1108 (2017). DOI:10.20959/wjpr20172-7838.

[38]. K. Jayanthi, R. P. Meena, K. Chithra, S. Kannan, W. Shanthi, R. Saravanan, M. Suresh, D. Satheesh, J. Pharm. Chem. Biol. Sci. 5, 205 (2017).

[39] N. Afsar, D. Reuben Jonathan, B.K. Revathi, D. Satheesh, S. Manivannan, (2E)-2-(4-ethoxybenzylidene)-3,4-dihydro-2H-naphthalen-1-one single crystal: Synthesis, growth,crystal structure, spectral characterization, biological evaluation and binding interactions with SARS-CoV-2 main protease, J. Mol. Struct,1244 (2021) 130967.

[40] N. Afsar, D. Reuben Jonathan, D. Satheesh, S. Manivannan, Computational description of quantum chemical calculations and pharmacological studies of the synthesized chalcone derivative: A promising NLO material, Journal of the Indian Chemical Society 99 (9), 2022, 100655.

[41] Yan, R., Zhang, Y., Li, Y., Xia, L., Guo, Y., Zhou, Q. (2020) Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science 367: 1444-1448.

[42] D. Satheesh, A. Rajendran, K. Chithra. Protein-ligand binding interactions of imidazolium salts with SARS CoV-2. Heliyon, 6, 2020, e05544.

[43] Dhurairaj Satheesh, Annamalai Rajendran, Kasi Chithra, Protein-Ligand Binding Interactions of 4-Nitroimidazolium Salts with Breast Cancer Protein: A Computational Biology Study, Asian J. Org. Med. Chem. 2022, 7(2), 163-173.