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Research Article

Synthesis of Schiff Bases 2-{[(4-Hydroxyphenyl) methylidene] amino} propanoic Acid, 4-[(Phenylimino)methyl] Phenol, and 4-{[(3-Chlorophenyl) methylidene] amino} Phenol and Molecular Docking Studies Against EGFR

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ABSTRACT

The implementation of green chemistry methods significantly reduces the amount of chemical waste. This study aimed to employ environmentally friendly techniques for synthesizing Schiff bases and evaluating their potential anticancer activity through molecular docking studies against EGFR. An innovative and sustainable condensation reaction was employed for the green synthesis of two Schiff bases, 4-[(phenylimino)methyl] phenol and 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid, whereas the third Schiff base, 4-{[(3-chlorophenyl) methylidene] amino} phenol, was synthesized using a conventional reflux method involving p-aminophenol and 3-chlorobenzaldehyde. The product was purified by basic filtration, washed with water, and dried. The synthesized compounds were characterized by their physical properties, melting points, TLC, FTIR, and ^{1}H NMR spectroscopy. The first Schiff base was a pale-yellow solid with a melting point of 190-196◦C; Rf: 0.83 (n-pentane: ethyl acetate, 1:3); yield: 62.7%). The second Schiff base after synthesis showed a light pink colour and was a crystalline solid with a melting point of 118-123◦C (Rf: 0.66 (n-pentane: ethyl acetate, 1:3)); the yield was 42.1%. The third Schiff base was orange-yellow in colour, solid in nature, with a melting point of 106-110◦C; Rf: 0.72 (n-pentane: ethyl acetate) and a yield of 58.2%. Molecular docking analysis suggested favourable interactions with the EGFR receptor via conventional hydrogen bonding at Thr766, which was similar to native ligand interactions with the receptor. The Schiff base exhibited a binding affinity of −6.7 kcal/mol and an RMSD value of 1.814 Å, indicating an acceptable docking pose.

Keywords: Schiff Base, para-aminophenol, 3-chlorobenzaldehyde, 4-[(phenylimino) methyl] phenol, 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid, Anticancer

1. INTRODUCTION

Coordination compounds have been extensively studied and are well understood; however, new advancements continue to emerge in this field of inorganic chemistry [1]. Historically, coordination compounds were regarded as rare and specialized; however, they

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are now recognized as highly versatile compounds that assist nature in transforming simple organic molecules into inorganic matter [2]. Schiff bases, containing an azomethine group (-HC=N-), are condensation products of ketones or aldehydes with primary amines, first reported by Hugo Schiff in 1864 [3]. Schiff base formation typically occurs under acid or base catalysis or with heat application. Common Schiff bases are crystalline solids, weakly basic, but some form insoluble salts with strong acids [4]. They are used as intermediates in amino acid synthesis or as ligands for preparing metal complexes with various structures. In addition, Schiff bases exhibit a range of biological activities, including antibacterial, antifungal, anticancer, and herbicidal properties [5].

Cancer is a multistage disease characterized by the uncontrolled proliferation of cells resulting from genetic alterations in normal cells [6]. These cells bypass cell-cycle checkpoints, evade apoptosis, proliferate uncontrollably, and invade surrounding tissues [7]. When a disease affects one part of the body, it can spread to other areas of the body. Early cancer detection allows for effective management and control [8]. Therefore, the identification of new compounds and methods to combat this problem is critical. Schiff bases have shown promising anticancer properties and may serve as potential therapeutic agents against cancer cells [9].

The traditional method for synthesizing imines involves mixing equimolar amounts of an aldehyde or ketone with a primary amine. The formation of imines is a reversible reaction that produces water [10]. When aromatic ketones react with primary amines, they require harsh conditions, such as a catalyst, longer reaction times, and higher temperatures, compared to aliphatic aldehydes, which often react spontaneously. Various catalysts, including $POCl_3$, BF_3, and acids, have been used to facilitate this reaction. [11]. Green chemistry employs techniques and processes that offer significant environmental and economic benefits compared to traditional synthetic methods. The increasing focus on green chemistry has led to the development of new organic synthesis methods that minimize the use of toxic organic solvents and chemicals [12]. These green methods aim to enhance selectivity, reduce reaction time, and simplify product isolation compared with conventional approaches [13]. Schiff base derivatives have been extensively studied for over a century and have been used in various fields, including magnetochemistry, nonlinear optics, photophysical studies, catalysis, materials chemistry, chemical analysis, and oxygen absorption and

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transport [14]. Given these advantageous properties, along with environmental concerns and a strong interest in green chemistry [15], new sustainable catalysts and environmentally friendly processes have been developed. These processes are both economically and technologically feasible and can be used as anticancer agents

The present study aimed to synthesize three Schiff base compounds, namely 4-[(phenylimino)methyl] phenol, 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid, and 4-{[(3-chlorophenyl) methylidene] amino} phenol, using environmentally friendly synthetic approaches. The synthesized compounds were characterized by their physical properties, melting points, thin-layer chromatography (TLC), Fourier-transform infrared (FTIR) spectroscopy, and ^{1}H NMR spectroscopy. In addition, molecular docking studies against the epidermal growth factor receptor (EGFR) were conducted to evaluate their potential interactions with a cancer-related molecular target. This work highlights the application of green chemistry principles in Schiff base synthesis and provides preliminary insight into their potential biological relevance.

2. EXPERIMENTAL SECTION

2.1. Materials

L-alanine, para-aminophenol, para-hydroxybenzaldehyde, 3-chlorobenzaldehyde, aniline, ethyl acetate, ethanol, dichloromethane, and n-hexane were procured from Sigma-Aldrich and used without additional purification.

2.2. General procedure for synthesizing Schiff bases using a green method

2.2.1. Procedure for the synthesis of 4-[(phenylimino) methyl] phenol

In a 250 mL conical flask, para-hydroxybenzaldehyde (0.24 g, 2 mmol) was dissolved in 20 mL of water, followed by the addition of aniline (0.2 mL, 2 mmol). The resulting mixture was stirred for 30 min at 25°C. The reaction progress was monitored by TLC every 10 min. The pale-yellow precipitate was collected by filtration, recrystallized from ethyl acetate, and dried at room temperature. The chemical reaction is shown in Figure 1.

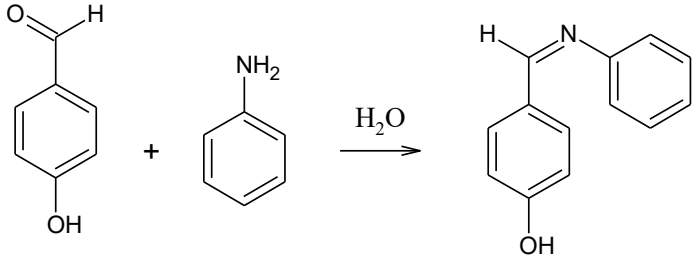

Figure 1. Synthesis of 4-[(phenylimino) methyl] phenol

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2.2.2. Synthesis of 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid

In a 250 mL conical flask, para-hydroxybenzaldehyde (1.2 g, 5 mmol) was dissolved in 20 ml of water, followed by the addition of L-alanine (0.35 g, 5 mmol). The resulting mixture was stirred for 2 h at 25°C. The reaction progress was monitored by TLC every 10 min. A light pink precipitate (0.32 g, 1.6 mmol, 42.1% yield) was formed, which was collected by filtration, recrystallized using ethanol, and dried at room temperature. The reaction scheme is shown in Figure 2.

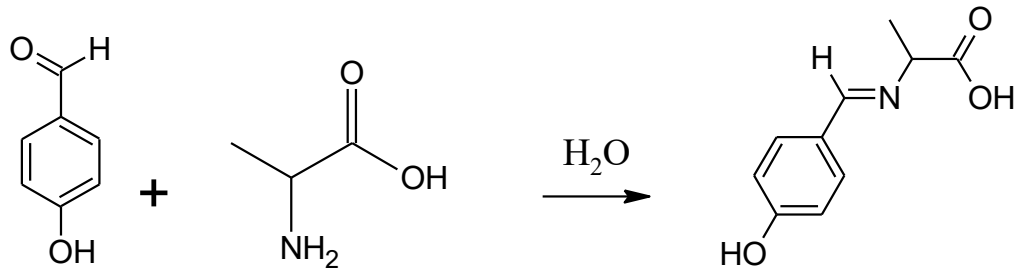

Figure 2. Synthesis of 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid

2.3. Synthesis of 4-{[(3-chlorophenyl) methylidene] amino} phenol through Conventional method

In a dry 250 mL round-bottomed flask, 3-chlorobenzaldehyde (0.3 mL, 3 mmol) and para-aminophenol (0.32 g, 3 mmol) were combined with 4 Å molecular sieves (8 g) in ethanol (30 ml) as the solvent. The reaction mixture was stirred continuously and refluxed for approximately 12–16 h until complete conversion was achieved, as monitored by TLC. The progress of the reaction was monitored by thin-layer chromatography (TLC) using precoated aluminum plates. After the reaction was complete, the mixture was allowed to cool to room temperature. Orange-yellow precipitates were formed and collected via filtration. The residue was washed with ethanol (3 × 100 mL). Upon adding 10 mL of dichloromethane (DCM) to the filtrate, orange-yellow imine crystals were formed along the sides of the container. Recrystallization was performed using n-hexane at room temperature. The chemical reactions are illustrated in Figure 3.

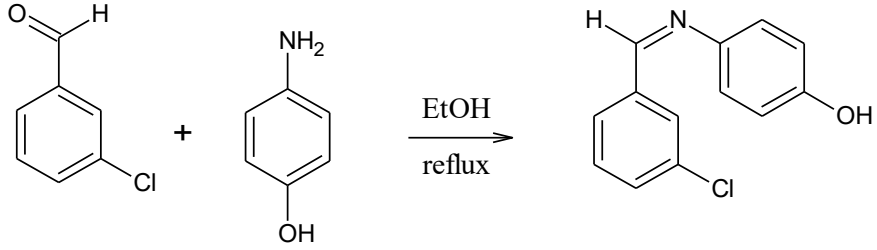

Figure 3. Synthesis of 4-{[(3-chlorophenyl) methylidene] amino} phenol

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2.4. Chromatographic technique

Thin-layer chromatography (TLC) was conducted using pre-coated silica gel aluminium plates (Merck) to monitor reaction progress and assess product purity. The mobile phase consisted of n-pentane: ethyl acetate (1:3, v/v). TLC spots were visualized under UV light at 254 nm. The solvents and reagents used were of analytical grade and obtained from Sigma-Aldrich and Merck and were used without further purification. Melting points were determined using a Gallen-Kamp apparatus.

2.5. In silico Analysis

The crystal structure of the receptor protein was obtained from the Protein Data Bank (PDB) (https://www.rcsb.org/structure page). The necessary receptor protein was prepared using Discovery Studio Software, water molecules were removed, and the native ligand was isolated from the receptor and saved in Pdbqt format. The native ligand and receptor were then redocked using the Auto Dock Tools 1.5.6 program, and the interactions, energy, and RMSD values were noted. The synthesized Schiff bases were docked against the EGFR receptor to evaluate their binding affinity and potential inhibitory interactions. EGFR (PDB ID: 1M17) was obtained from the RCSB PDB Protein Data Bank.

3. RESULTS AND DISCUSSION

3.1. 4-[(phenylimino) methyl] phenol

For thin-layer chromatography (TLC), a silica plate obtained from Merck was used as the stationary phase. The mobile phase consisted of n-pentane and ethyl acetate (1:3, v/v). TLC analysis confirmed the complete consumption of aniline during Schiff base formation, with Rf values of 0.64 for aniline and 0.83 for the Schiff base.

3.2. 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid

A silica plate from Merck was employed as the stationary phase, and the mobile phase consisted of n-pentane and ethyl acetate (1:3, v/v). TLC analysis confirmed the complete consumption of L-alanine in the Schiff base synthesis, with Rf values of 0.45 for L-alanine and 0.66 for the Schiff base.

3.3. 4-{[(3-chlorophenyl) methylidene] amino} phenol

A commercially available silica plate (Merck) served as the stationary phase, with a mobile phase composed of n-pentane and ethyl acetate (1:3, v/v). TLC analysis indicated the

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complete utilization of p-aminophenol in the synthesis of the Schiff base, yielding Rf values of 0.45 for p-aminophenol and 0.62 for the Schiff base.

3.4. Spectroscopic results

3.4.1. 4-[(phenylimino) methyl] phenol

The presence of a C=N bond (imine) at 1670 cm^{-1} in the IR spectrum and a singlet at 8.39 ppm in the ^1H NMR spectrum for the proton attached to the imine nitrogen are key indicators of Schiff base formation. The aromatic C=C bonds are also evident in the IR spectrum at 1561 and 1512 cm^{-1}. The singlet at 5.00 ppm in the ^1H NMR spectrum suggests a proton attached to an OH group, which could be part of the starting material or the product itself [16]. The Rf value of 0.83 obtained using a mobile phase of n-pentane: ethyl acetate (1:3) indicates that the compound migrated significantly on the silica gel plate under the selected chromatographic conditions. The observed Rf value can be used as a characteristic parameter for monitoring reaction progress and assessing product purity, as shown in Figure 4.

Yellow crystalline solid (62.7%): m.p 190-196°C; Rf: 0.83 (n-pentane: ethyl acetate, 1:3) IR (pure, cm-1): 1670 (N=C), 1561, 1512 (C=C), 1264 (C-O). 1HNMR (DMSO-d6, 400 MHz): δ 8.39 (s, 1H(Hd), N=CH), 7.45 (d, 2H(Hc), Ar), 7.3 (m, 5H(He), Ar), 6.76 (d, 2H(Hb), Ar), 5.0 (s, 1H(Ha), OH).

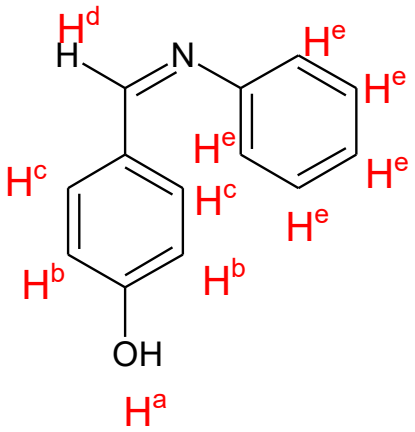

Figure 4. Characterization of 4-[(phenylimino) methyl] phenol

3.4.2. 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid

The product was obtained as a light-pink crystalline solid at room temperature. The Rf value provides information regarding the chromatographic behaviour of the compound. The Rf value of 0.66 obtained using n-pentane: ethyl acetate (1:3) reflects the chromatographic

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behaviour of the compound on silica gel and confirms its separation from the starting materials. The value is useful for reaction monitoring and purity assessment [17]. The presence of the Schiff base was confirmed by the C=N stretching vibration at 1675 cm^{-1} in the IR spectrum and a singlet at 8.11 ppm in the ^1H NMR spectrum corresponding to the imine proton. The aromatic C=C bonds and OH group are also evident, as shown in Figure 5.

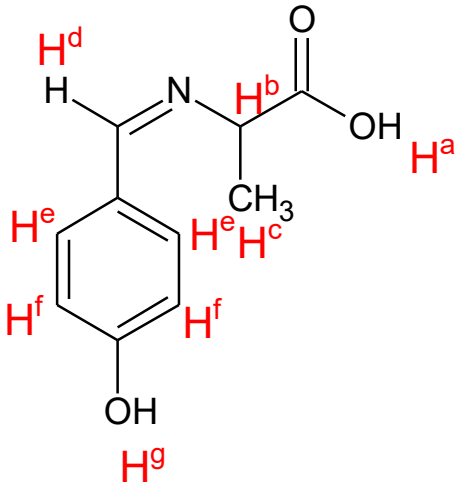

Figure 5. Characterization of 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid

Light pink crystalline solid (42.1%): m.p 118-123°C; Rf: 0.66 (n-pentane: ethyl acetate, 1:3) IR (pure, cm^{-1}): 1675 (N=C), 1568, 1513 (C=C), 1260 (C-O). 1HNMR (DMSO-d6, 400 MHz): δ 11.0 (s, 1H(Ha), COOH), 8.11 (s, 1H(Hd), N=CH), 7.45 (d, 2H(He), Ar), 6.76 (d, 2H(Hf), Ar), 5.0 (s, 1H(Hg), OH), 4.18 (q, 1H(Hb), CH), 1.41 (d, 3H(Hc), CH_3).

The singlet observed at 11.0 ppm corresponds to the carboxylic acid proton, confirming the presence of the carboxylic acid functionality inherited from the L-alanine precursor. The quartet observed at 4.18 ppm corresponds to the α-methine proton (CH) of the alanine moiety, while the doublet at 1.41 ppm corresponds to the adjacent methyl group (CH_3). The observed coupling pattern is consistent with the structure of 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid and supports successful Schiff base formation.

3.4.3. 4-{[(3-chlorophenyl) methylidene] amino} phenol

The compound exhibited an Rf value of 0.62 in n-pentane: ethyl acetate (1:3), indicating effective migration on the silica gel plate under the selected chromatographic conditions. The Rf value served as a useful parameter for monitoring the reaction and evaluating product purity. 1670 cm^{-1}: This peak corresponds to the stretching vibration of the C=N bond (imine functional group), a key characteristic of Schiff bases 1565 and 1511 cm^{-1}: These peaks

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indicate the presence of aromatic C=C bonds. 1260 cm^{-1}: This peak might be due to C-O stretching vibration, possibly from a phenol or alcohol group in the molecule [18]. More details are given below in Figure 6.

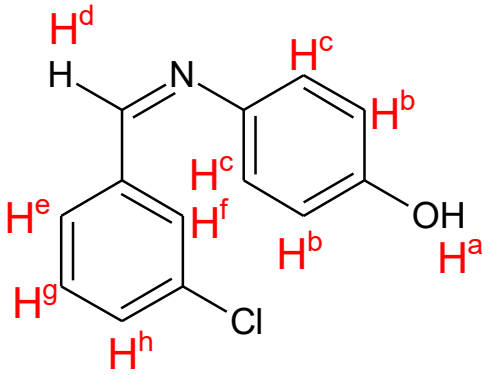

Figure 6. Characterization of 4-{[(3-chlorophenyl) methylidene] amino} phenol

Orange-yellow crystalline solid (58.2%): m.p 106-110°C; Rf: 0.62 (n-pentane: ethyl acetate, 1:3) IR (pure, cm^{-1}): 1670 (N=C), 1565, 1511 (C=C), 1260 (C-O). 1HNMR (DMSO-d6, 400 MHz): δ 8.39 (s, 1H(Hd), N=CH), 7.63 (s, 1H(Hf), Ar) 7.50 (d, 1H(He), Ar), 7.30 (d, 1H(Hh), Ar), 7.23 (t,1H(Hg), Ar), 7.1 (d, 2H(Hc), Ar), 6.7 (d, 2H(Hb), Ar), 5.0 (s, 1H(Ha), OH).

The interesting feature here is the presence of a singlet peak at 7.63 ppm in the ^{1}H NMR spectrum. This suggests a specific arrangement of substituents on the aromatic ring where a proton has a unique chemical environment compared to the others. Analysing the splitting patterns of the other aromatic protons (7.50, 7.30, 7.23, 7.1 ppm) along with the knowledge of starting materials used in the synthesis could help identify the specific substitution pattern on the aromatic ring.

3.5. In silico study results

The native ligand exhibited a strong interaction with the receptor through a conventional hydrogen bond involving the Thr766 residue. In addition, several van der Waals interactions were observed, van der Waals interactions occurred at Gly695, Phe699, Gly772, Pro770, Leu764, Lys721, Glu738, Met742, Thr830, Asp831, Gln767, Met769 and Leu768. In addition, ionic interactions were observed with several amino acid residues. During AutoDock Vina analysis, 20 docking poses were generated. The best pose exhibited an RMSD value of 1.846 Å and a binding affinity of −5.8 kcal/mol. The interactions, RMSD value, and binding affinity of the native ligand with the receptor are presented in Figure 7.

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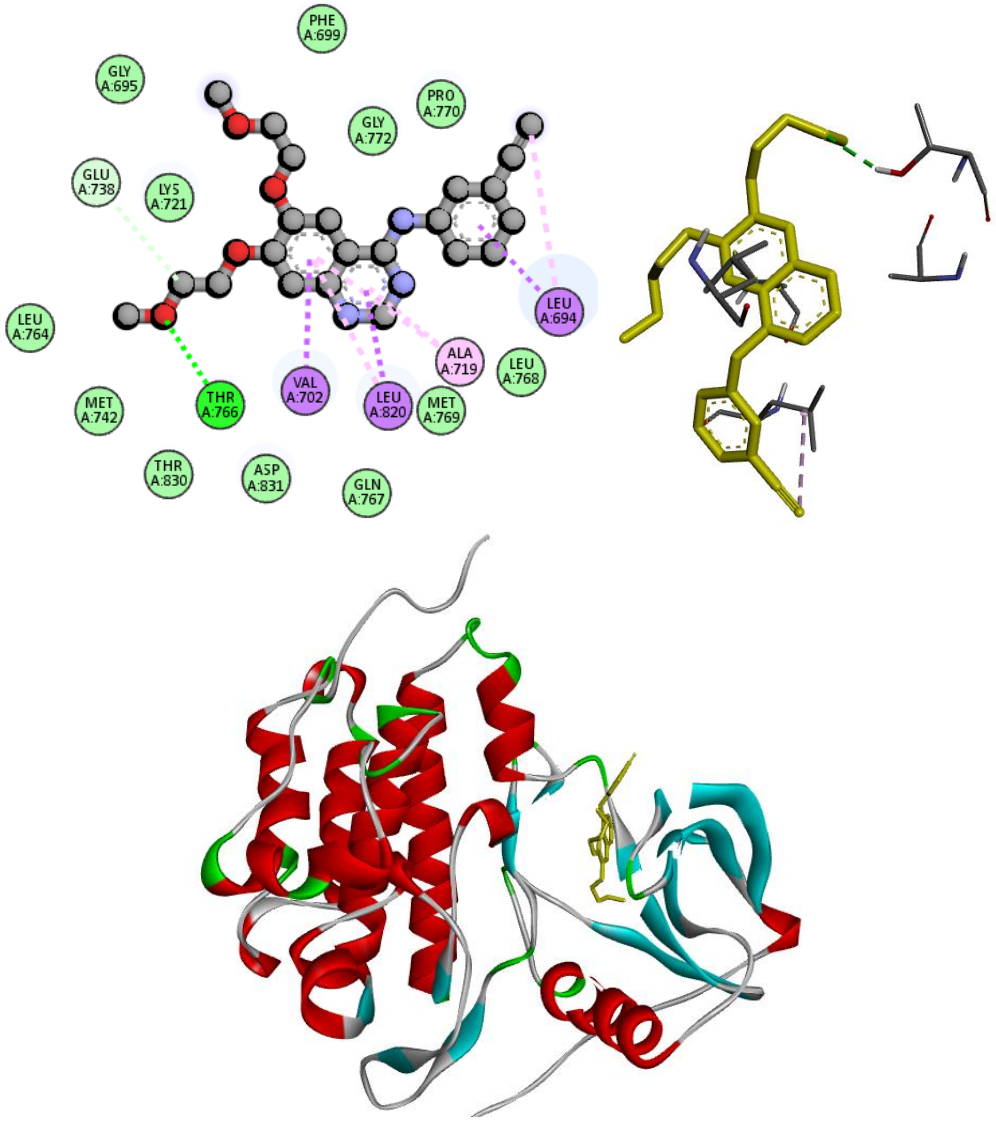

Figure 7. Native ligand interactions with receptor

The Schiff base exhibited strong interactions with the EGFR receptor, suggesting potential interaction with the EGFR target and warranting further biological investigation, similarly in previous research peptides from *Naja Sumatrana* venom [19] as well as peptides from *Naja Kaouthia* venom peptides [20]. The Schiff base formed three conventional hydrogen bonds with residues Ala719, Lys721, and Thr766, as shown in Figure 8, and one is similar with native ligand Thr766 which suggests that the Schiff base may occupy a binding region similar to that of the native ligand. Interestingly, the Schiff base formed more conventional hydrogen bonds than the native ligand which suggests favourable ligand–receptor interactions [21].

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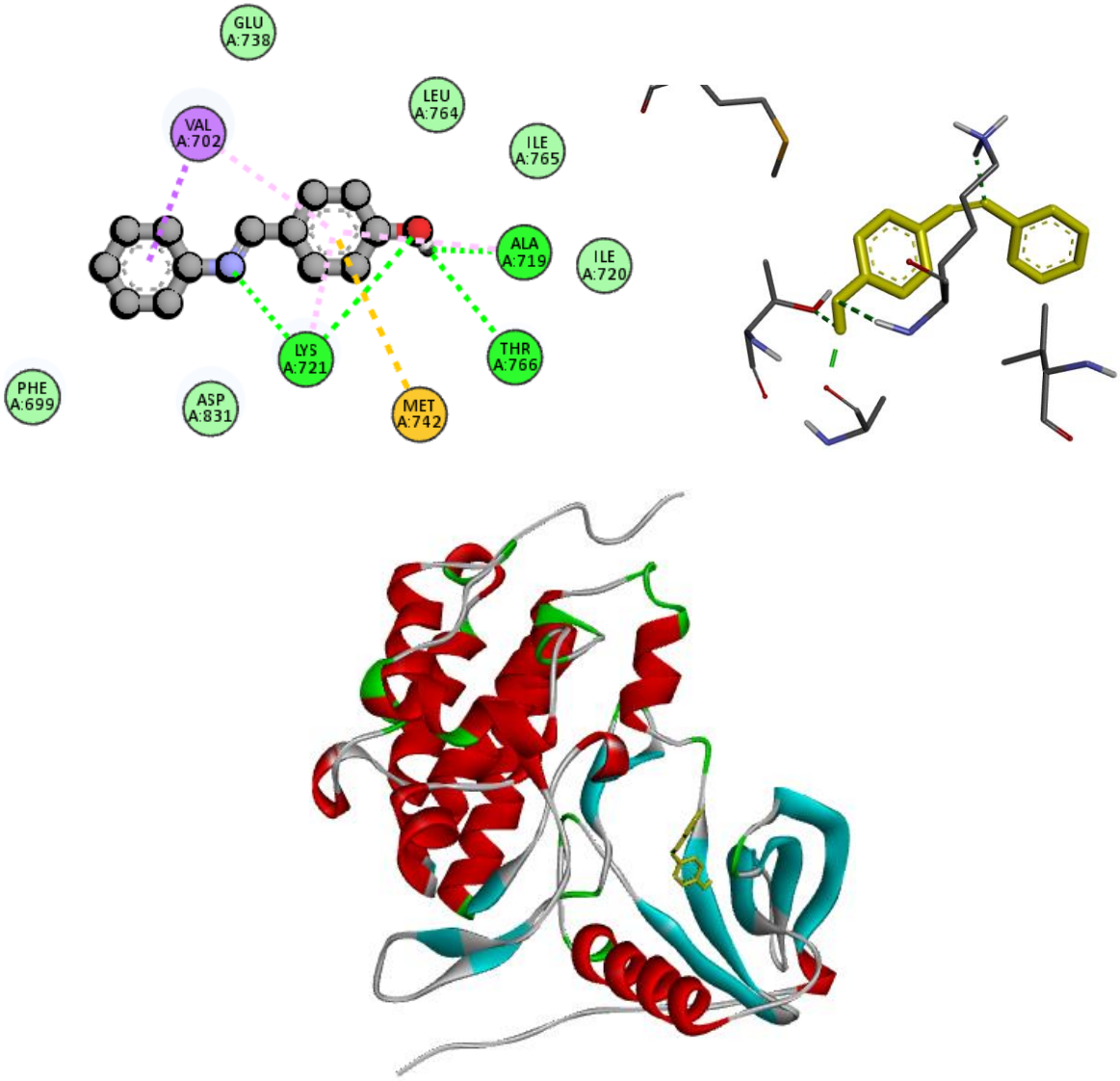

Figure 8. Interactions of Schiff base with Receptor

Other interactions exhibited by the Schiff base with the receptor were Glu738, Leu764, Ile765, Ile720, Asp831 and Phe699 which may further contribute to the stability of the ligand–receptor complex [22]. Besides these interactions, other criteria used to evaluate docking performance include RMSD and binding affinity. An RMSD value below 2 Å is generally considered acceptable for docking validation [23].

Table 1. RMSD and affinity score of Native ligand and Schiff base with receptor

No	Ligand	RMSD (Å)	Affinity (kcal/mol)
1	Native Ligand	1.846	-5.8
2	Schiff Base	1.814	-6.7

Binding energy is another important parameter, and lower binding energy values generally indicate stronger ligand–receptor interactions. In this study, the Schiff base exhibited a binding affinity of −6.7 kcal/mol, which was lower than that of the native ligand

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(−5.8 kcal/mol) as shown in Table 1, suggesting a favourable ligand–receptor interaction. The RMSD value of 1.814 Å was below the commonly accepted threshold of 2 Å, indicating a reliable docking pose and acceptable conformational stability. Binding affinity reflects the predicted strength of ligand–receptor interactions, whereas RMSD is used to evaluate the reliability and reproducibility of the docking orientation [24]. Collectively, these results suggest that the Schiff base possesses favourable binding characteristics toward EGFR and may serve as a promising scaffold for further investigation, although experimental validation is required to confirm its biological activity.

4. CONCLUSION

Three Schiff base compounds, namely 4-[(phenylimino)methyl] phenol, 2-{[(4-hydroxyphenyl) methylidene] amino} propanoic acid, and 4-{[(3-chlorophenyl) methylidene] amino} phenol, were successfully synthesized using an environmentally friendly aqueous condensation method under mild reaction conditions. The synthesized compounds were characterized by TLC, FTIR, and ^{1}H NMR spectroscopy, confirming the successful formation of the Schiff base functionality. The use of water as a green solvent demonstrates a simple, cost-effective, and sustainable approach for Schiff base synthesis. Molecular docking studies against EGFR revealed favourable ligand–receptor interactions, suggesting that the synthesized Schiff bases possess potential biological relevance and may serve as promising scaffolds for the development of future EGFR-targeted compounds. However, further in vitro and in vivo studies are required to validate the biological activity predicted by the docking analysis.

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CONFLICT OF INTERESTS

The authors declare there are no financial or personal relationships that could present a potential conflict of interests.

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REFERENCES

[1] Raczuk, E., Dmochowska, B., Samaszko-Fiertek, J. & Madaj, J. (2022). Different Schiff Bases—Structure, Importance and Classification. *Mol. 2022 Vol 27 Page 787*, 27 (3), 787.

[2] Yang, L., Cui, Y., Shen, J., Lin, F., Wang, X., Long, M., Wei, J. & Zhang, H. (2015). Antitumor activity of SA12, a novel peptide, on SKBr-3 breast cancer cells via the mitochondrial apoptosis pathway. *Drug Des. Devel. Ther.*, 9, 1319–1330.

[3] Dapson, R.W. (2016). Schiff and pseudo-Schiff reagents: the reactions and reagents of Hugo Schiff, including a classification of various kinds of histochemical reagents used to detect aldehydes. *Biotech. Histochem.*, 91 (8), 522–531.

[4] Zhou, P., Li, B., Yan, Y., Jin, B., Wang, L. & Huang, S.Y. (2018). Hierarchical Flexible Peptide Docking by Conformer Generation and Ensemble Docking of Peptides, 2018.

[5] Uddin, N., Rashid, F., Ali, S., Tirmizi, S.A., Ahmad, I., Zaib, S., Zubair, M., Diaconescu, P.L., Tahir, M.N., Iqbal, J. & Haider, A. (2020). Synthesis, characterization, and anticancer activity of Schiff bases. *J. Biomol. Struct. Dyn.*, 38 (11), 3246–3259.

[6] Patsadu, O., Tangchitwilaikun, P. & Lowsuwankul, S. (2021). Liver Cancer Patient Classification on a Multiple-Stage using Hybrid Classification Methods. *Walailak J. Sci. Technol. WJST*, 18 (10), Article 9169 (14 pages).

[7] Herrmann, A., Rice, M., Lévy, R., Pizer, B.L., Losty, P.D., Moss, D. & Sée, V. (2015). Cellular memory of hypoxia elicits neuroblastoma metastasis and enables invasion by non-aggressive neighbouring cells. *Oncog. 2015 42*, 4 (2), e138–e138.

[8] Fadelu, T. & Rebbeck, T.R. (2021). The rising burden of cancer in low– and middle–Human Development Index countries. *Cancer*, 127 (16), 2864–2866.

[9] Tadele, K.T. & Tsega, T.W. (2019). Schiff Bases and their Metal Complexes as Potential Anticancer Candidates: A Review of Recent Works. *Anticancer Agents Med. Chem.*, 19 (15), 1786–1795.

[10] Patil, R.D. & Adimurthy, S. (2013). Catalytic Methods for Imine Synthesis. *Asian J. Org. Chem.*, 2 (9), 726–744.

[11] Morales, S., Guijarro, F.G., García Ruano, J.L. & Cid, M.B. (2014). A general aminocatalytic method for the synthesis of aldimines. *J. Am. Chem. Soc.*, 136 (3), 1082–1089.

[12] Mehdi, K., Khan, S., Ali, A., Badshah, K. & Ahmed, N. (2023). Green Synthesis of Silver and Gold Nanoparticles Using Tradescantia Pallida Extract: Their Characterization and Antimicrobial Activity, in: *Inclusiveness Digit. Transform. Renew. Energy Better Future*, PROCEEDING AL GHAZALI International Conference, Cilcap, 2023: pp. 132–145.

[13] Ahmad, K., Warsito, B., Hidayat, J.W., Khan, S., Ahmed, N., Calvin, E.J. & Ashraf, M. (2023). Green synthesis of silver nanoparticles and degradation of AZO-dyes using Cestrum diurnum plant extract, and antimicrobial activities of AgNP's. *J. Bioresour. Environ. Sci.*, 2 (2), 78–88.

[14] Boulechfar, C., Ferkous, H., Delimi, A., Djedouani, A., Kahlouche, A., Boublia, A., Darwish, A.S., Lemaoui, T., Verma, R. & Benguerba, Y. (2023). Schiff bases and their metal Complexes: A review on the history, synthesis, and applications. *Inorg. Chem. Commun.*, 150, 110451.

[15] Mermer, A., Demirbas, N., Uslu, H., Demirbas, A., Ceylan, S. & Sirin, Y. (2019). Synthesis of novel Schiff bases using green chemistry techniques; antimicrobial, antioxidant, antiurease activity screening and molecular docking studies. *J. Mol. Struct.*, 1181, 412–422.

***Submitted**: 2026-04-29; **Accepted**: 2026-06-17; **Published**: 2026-07-01*

[16] Ortegón-Reyna, D., Garcías-Morales, C., Padilla-Martínez, I., García-Báez, E., Aríza-Castolo, A., Peraza-Campos, A. & Martínez-Martínez, F. (2013). NMR Structural Study of the Prototropic Equilibrium in Solution of Schiff Bases as Model Compounds. *Mol. 2014 Vol 19 Pages 459-481*, 19 (1), 459–481.
[17] Kamaria, P., Kawathekar, N. & Chaturvedi, P. (2011). Microwave Assisted Synthesis and Antimicrobial Evaluation of Schiff Bases of Indole-3-aldehyde. *J. Chem.*, 8 (1), 305–311.
[18] Berber, N., Arslan, M., Schiff, B., Bileşiklerinin, B., Ve, H. & Öz, K. (2020). Preparation and Characterization of Some Schiff Base Compounds. *Adıyaman Univ. J. Sci.*, 10 (1), 179–188.
[19] Ahmed, N., Erlista, G.P., Raharjo, T.J., Swasono, R.T. & Raharjo, S. (2023). Anticancer Activity of Venom Protein Hydrolysis Fraction of Equatorial Spitting Cobra (Naja sumatrana). *Indones. J. Chem.*, 23 (2), 510–522.
[20] Erlista, G.P., Ahmed, N., Swasono, R.T., Raharjo, S. & Raharjo, T.J. (2023). Proteome of monocled cobra (Naja kaouthia) venom and potent anti breast cancer peptide from trypsin hydrolyzate of the venom protein. *Saudi Pharm. J.*, 31 (6), 1115–1124.
[21] Li, P., Niu, M.J., Hong, M., Cheng, S. & Dou, J.M. (2014). Effect of structure and composition of nickel(II) complexes with salicylidene Schiff base ligands on their DNA/protein interaction and cytotoxicity. *J. Inorg. Biochem.*, 137, 101–108.
[22] Williams, M.A., Goodfellow, J.M. & Thornton, J.M. (1994). Buried waters and internal cavities in monomeric proteins. *Protein Sci.*, 3 (8), 1224–1235.
[23] Kaur, S., Modi, N.H., Panda, D. & Roy, N. (2010). Probing the binding site of curcumin in Escherichia coli and Bacillus subtilis FtsZ - A structural insight to unveil antibacterial activity of curcumin. *Eur. J. Med. Chem.*, 45 (9), 4209–4214.
[24] Xu, Y., Kalra, T.S., Ganju, N.K. & Fagherazzi, S. (2022). Modeling the Dynamics of Salt Marsh Development in Coastal Land Reclamation. *Geophys. Res. Lett.*, 49 (6), e2021GL095559.

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