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SYNTHESIS, DOCKING STUDIES AND ANTIMICROBIAL AND ANTIOXIDANT ACTIVITY OF THIAZOLE SCHIFF BASE DERIVATIVES

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ABSTRACT: Fifteen Thiazole Schiff bases derivatives were synthesized, designed and evaluated for antimicrobial and antioxidant activity. Based on literature review compounds were synthesized, docked and tested for All biological assays were performed in triplicate (n = 3). Positive controls: Ciprofloxacin (10 µg/mL) for antibacterial and Ketoconazole (10 µg/mL) for antifungal assays. Results are expressed as mean ± SD and for antioxidant properties DPPH assay, ABTS [2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)] assay, Ferric Reducing Antioxidant Power Assay and Hydrogen peroxide (H_2O_2) scavenging assay were employed. Molecular docking was performed against topoisomerase II, peptide deformylase, lanosterol 14α-demethylase, and tyrosinase enzymes, which revealed favourable binding affinities and hydrogen-bonding interactions with the respective active sites for several derivatives. Compounds TSB_S7, TSB_S8, TSB_S10 and TSB_S14 exhibited the highest MolDock scores and showed MIC (µg/mL) values of 25 µg/mL against *S. aureus* and *E. coli*. The compounds were more active against Gram-positive than Gram-negative bacteriaria than Gram negative bacteria. The compounds demonstrated promising antibacterial and antioxidant properties with MICs ranging from 25 to 50 µg/ml. Overall, the synthesized thiazole Schiff bases demonstrated dual antimicrobial and antioxidant properties, highlighting their potential as multifunctional therapeutic agents.

INTRODUCTION: According to WHO, "Antimicrobial agents include antibiotics, antifungals and antiparasitic, medicines employed to prevent and treat infections in humans, animals and plants" [1]. Antibiotics among the antimicrobials remained extensively used to control infective diseases. The effective use of antibiotics is challenged by the quick advent of antibiotic resistance and the requirement for better methods of delivery [2].

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To control drug resistance, novel antimicrobial agents are required to which the experimental isolated microbes cannot easily acquire resistance [3]. Cell wall, protein and nuclei acid synthesis inhibitors, depolarize the cell membrane and metabolic pathways which inhibits microbes to get inside the body. Antioxidants reduce free radical producing enzymes for example NAD (P)H, xanthine oxidase [4].

Vitamin C scarcity leads to anaemia and it's a natural antioxidant strengthen folate by absorbing soluble non-haem iron by chelation and kept in reduced (ferrous, Fe^{2+}) form and elimination of oxidized folate derivatives was reduced [5]. Antioxidant therapy has been appreciated as it can decrease the hazard of cancer and several cardiac

disorders and thiazole is fundamental structure of a variety of drugs [6]. Suspension of lipid peroxidation and prevention of radical chain reactions, leading to the amelioration of food and pharmaceutical products at processing and storage stage [7]. *In-vitro* antimicrobial assay can be performed using methods such as agar well diffusion method [8], antioxidant assays evaluation method for antioxidant ability should be rapid, consistent and less concentration should be required for its analysis [9]. The activity of each antioxidant which can terminate radical chain processes cannot be evaluated directly So, to find out activity of each active compounds in the biological extracts of complexes a fast and precise method of ELISA microplate reader with 96 well plate with different reagents such as DPPH radical, FRAP, ABTS are presently used for rapid screening of active compounds. The first imine was reported in the 19th century by Hugo Schiff (1864) by the reaction of primary amines with carbonyl compounds [10]. These compounds are also recognized as anils, imines or azomethines, thiazole Schiff bases are formed by the condensation of arylamines and carbonyl compounds [11, 12]. Further, a range of approaches for the formation of imines have been defined [13]. Schiff base is described as a group comprising of an imine or azomethine (−CH = N−) group, are usually formed by the condensation reaction of carbonyl compounds (aldehyde or ketone) with compounds containing of amine group and show antimicrobial and antioxidant properties [14, 15]. Mechanism of action of antioxidant activity is due to their capability to reduce free radicals and reversibly bound with redox system of biochemical and cellular reactions [16].

MATERIALS AND METHODS: Based on review of literature done Synthesis of thiazole Schiff base derivatives for their antimicrobial and antioxidant properties was done. For more potency and selectivity substitution of phenyl Schiff base (imine moiety) was done. Design, molecular docking studies were done for structural and chemical properties of the molecule as shown in **Fig. 1.**

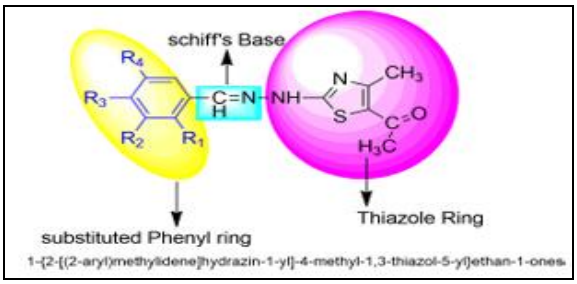


FIG. 1: FIG. 1: BASIC NUCLEUS SHOWING THREE PHARMACOPHORES OF THE THIAZOLE SCHIFF BASE (LABELS INDICATE PHARMACOPHORE REGIONS)

Chemistry: All chemical substances and reagents were of synthetic grade. The reactions took place using distilled and dried solvents and progress was observed via Thin layer chromatography (TLC) and visualized using iodine chamber. Melting point was determined using Digital Veego Model melting point apparatus.

Synthesis: Condensation reaction of substituted benzaldehydes and thiosemicarbazide gives Benzaldehyde thiosemicarbazones 1a-1o. Compounds TSB_S1- TSB_S15 formed by intramolecular addition between 1a-1o and 3-chloroacetylacetone as shown in **Fig. 2** with yield of 51.9–97%.

Procedure: Substituted benzaldehyde (5.0 m mole) were reacted with thiosemicarbazide (0.455 g, 5.0 mmole) in the presence of ethanol 25.0 mL and then subjected to reflux at 80°C, continuously stirred till completion on magnetic stirrer for 10–20 minutes confirmed by glass coated TLC plate coated with silica gel-G with solvents chloroform and methanol in a ratio of 7:3 v/v, and results were detected by iodine vapour chamber, Once the reaction was completed, the reaction mixture was cooled to room temperature, filtered to acquire the intermediate product, and then recrystallized from ethanol to produce substituted benzaldehyde thiosemicarbazones.

In second step Benzaldehyde thiosemicarbazone (2 mmole) and 3-chloro acetyl acetone (2 mmole) were subjected to reflux at 80°C (magnetic stirrer were used) reaction progress was checked by TLC,

the mixture was cooled at 25°C, after completion the crude precipitate was filtered with Whatman filter paper, dried and recrystallized with ethanol to yield final product of substituted thiazole Schiff bases [6].

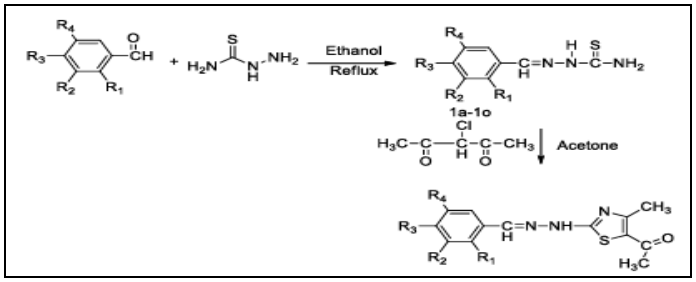


FIG. 2: SYNTHESIS SCHEME

TSB_S1- 1-{2-[2-[(2-hydroxy, 5-nitrophenyl) methylidene] hydrazin-1-yl]−4- methyl-1,3thiazol-5-yl}ethan-1-one: Orange powder; Yield (93.02%); m.p. 78 ℃; UV (*λ*max, nm); FTIR ((*u*, cm^{-1}) 739 [C-S-C str.], 1250 [C-O str.], 1545 [N=O Ar str.], 1577 [C=C (Ar str.)], 1675 [C=O str.(thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.], 3300 [O-H str.], 3436 [N-H str.]; 1H-NMR (δ ppm) (CDCl3)- 2.2 (s, 3H, thiazole-CH3), 2.50(s, 3H, thiazole- COCH3), 4.0 (s, 1H, N-H), 5 (s, 1H, OH), 7.0 (d, 1H, m-Ar-H), 8.1 (s, 1H, N=C-H), 8.2 (d, 1H, p-Ar-H), 8.4 (s,1H, o-Ar-H); M wt. (g/mol) 320.32, C13H12N4O4S, HRMS: m/z 319 (M-1).

TSB_S2- 1-{2-[2-[(5-bromo, 4-hydroxyphenyl) methylidene] hydrazin-1- yl]−4-methyl-1,3 thiazol-5-yl}ethan-1-one: Yellow crystal, Yield (93.02%); m.p 150℃; UV (*λ*max, 335nm); IR (KBr) cm-739 [C-S-C str.], 1032 [C-Br str.], 1250 [C-O str.], 1577 [C=C (Ar str.)], 1675 [C=O str. (thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.], 3300 [O-H str.], 3436 [NH str.]; 1H-NMR (δ ppm) (CDCl3)- 2.47 (s, 3H, thiazole-CH3), 2.55 (s, 3H, thiazole- COCH3), 4.0 (s, 1H, N-H), 5 (s, 1H, OH), 6.7 (d, 1H, m-Ar-H), 7.6 (d, 1H, o-Ar-H), 8.1 (s, 1H, N=C- H); M wt. (g/mol) 354.24, C13H14BrN3O2S, HRMS 353 (M-1), 356 (M+2).

TSB_S3- 1-{2-[2-[(3-diethylaminophenyl) methylidene] hydrazin-1-yl]−4-methyl- 1,3 thiazol-5-yl} ethan-1-one: Brown crystal, Yield (51.9%); m.p. 195℃; UV (*λ*max, 339nm); IR (KBr) cm-739 [C-S-C str.], 1032 [C-Br str.], 1250 [C-O str.], 1577 [C=C (Ar str.)], 1675 [C=O str. (thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.], 3300 [O-H str.], 3436 [NH str.]1H-NMR (δ ppm) (CDCl3) 2.47 (s, 3H, thiazole-CH3), 2.55 (s, 3H, thiazole- COCH3), 4.0 (s, 1H, N-H), 5 (s, 1H, OH), 6.7 (d, 1H, m-Ar-H), 7.6 (d, 1H, o-Ar-H), 8.1 (s, 1H, N=C-H); M wt. (g/mol) 354.24; C13H14BrN3O2S; HRMS 353 (M-1), 356 (M+2).

TSB_S4- 1-{2-[2-[(2-ethoxyphenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3-thiazol-5yl} ethan-1-one: Yellow crystal , yield (92%); m.p 163℃; UV (*λ*max, 322nm); IR (KBr) cm-739 [C-S-C str.], 1250 [C-O str.],1264 [C-O str., (OCH3)], 1577 [C=C Ar str.], 1675 [C=O str. (thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.], 3436 [N-H str.] 1H-NMR (δ ppm) (CDCl3) 1.33 (t, 3H, CH3 of ethoxy), 2.47 (s, 3H, thiazole- CH3), 2.55 (s, 3H, thiazoleCOCH3), 4.0 (s, 1H, N- H), 4.5 (q, 2H, CH2 of ethoxy), 7.2 (d, 1H, p-Ar-H), 7.5 (d, 1H, o-ArH), 6.8 (s, 1H, m-Ar-H), 8.1 (s, 1H,N=C-H); M wt. (g/mol) 303.38, C17H24N4O2S, HRMS 303(M+).

TSB_S5- 1-{2-[2-[(2-ethoxyphenyl) methylidene] hydrazin-1-yl]−4-methyl 1,3thiazolyl}ethan-1-one: Yellow crystal, yield (89%); m.p 85℃; UV (*λ*max, 337nm), FTIR (*u*, cm-1)- 739 [C-S-C str.], 1250 [C-O str.], 1577 [C=C (Ar str.)],1675 [C=O str. (thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.], 3300 [O-H str.], 3436 [N-H str.]; M wt. (g/mol) 291.34; C13H15N3O3S , HRMS 292 (M+1).

TSB_S6- 1-{2-[2-[(4-hydroxy, 3-methoxy phenyl) methylidene] hydrazin-1-yl]−4- methyl1,3-thiazol-5-yl} ethan-1-one: Brown Greenish powder yield (92.7%); m.p. 75℃; UV (*λ*max, 328nm), FTIR (*u*, cm-1)- 728 [C-S-C str.], 1250 [C-O str.], 1270 [C-O str.,OCH3], 1583 [C=O str. (thiazole)], 1583 [C=C Ar str.], 1630 [N=C-H str. (imine)], 3276 [C-H str.], 3300 [OH str.], 3436 [N-

H str.] , M wt. (g/mol) 305.37, C14H17N3O3S, HRMS 305(M+).

TSB_S7- 1-{2-[2-[(3-bromophenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3-thiazol5yl} ethan-1-one: Yellow crystal powder yield (85%); m.p. 150℃; UV (*λ*max, 327nm), FTIR (*u*, cm-1)- 750 [C-S-C str.], 1258 [C-O str.], 1032 [C-Br str.], 1563 [C=O str. (thiazole)], 1599 [C=C (Ar str.)], 1630 [N=C-H str. (imine)],3010 [C-Hstr.], 3436 [N-H str.], 3436 [N-H str.], M wt. (g/mol) 338.24, C13H14BrN3OS, HRMS 340(M+2).

TSB_S8- 1-{2-[2-[(4-aminophenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3- thiazol-5yl} ethan-1-one: Orange crystal powder; yield (76%); m.p. 158℃; UV (*λ*max, 373nm); FTIR (*u*, cm-1)- 542 [C-S-C bend], 1259 [C-O str., (Ar-OCH3)], 1594 [C=C (Ar str.)], 1594 [C=O str.(thiazole)], 1647 [N=C-H str. (imine)], 3010 [C-H str.], 3436 [N-H str.], 3500 [HN-H str.]; M wt. (g/mol) 274.36; C13H16N4OS, HRMS 273(M-1).

TSB_S9- 1-{2-[2-[(3-hydroxy, 4-methoxyphenyl) methylidene] hydrazin-1-yl]−4- methyl1,3-thiazol-5-yl}ethan-1-one: Yellow crystal powder; yield (72%); m.p. 150℃; UV (*λ*max, 380nm); FTIR (*u*, cm-1)- 734 [C-S-C str.], 1253 [C-O str., (Ar-OCH3)],1270 [Ar-OCH3)], 1573 [C=C Ar str.],1573[C=O str. (thiazole)], 1600 [N=C-H str. (imine)], 2840 [C-H str.], 3125 [O-H str.], 3425[N-H str.]; M wt. (g/mol) 305.37; C14H17N3O3S, HRMS 305(M)+.

TSB_S10 - 1 - {2 - [2 - [(4 - hydroxyphenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3-thiazol5-yl} ethan-1-one: Purple crystal powder; yield (88%); m.p. 170℃; UV (*λ*max, 340nm); FTIR (*u*, cm-1)- 716 [C-S-C str.], 1220 [C-O str., (Ar-OCH3)],1580 [C=O str. (thiazole)], 1600 [N=C-H str. (imine)], 1610 [C=C Ar str.], 2922 [C-H str.], 3010 [O-H str.], 3050 [C-H str.], 3436 [N-Hstr.]; M wt. (g/mol) 275.33; C13H13N3O2S; HRMS 274(M-1).

TSB_S11- 1-{2-[2-[(2-ethylphenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3-thiazol-5yl} ethan-1-one: Brown crystal powder, yield (86%); m.p. 60℃; UV (*λ*max, 325nm), FTIR (*u*, cm-1)- 736 [C-S-C str.], 1227 [C-O str., (Ar-OCH3)],1375 [CH3 bend], 1561 [N=C-H str. (imine)], 1593 [C=C Ar str.], 1635 [C=O str. (thiazole)], 2963 [sp3 C-H str.], 3436 [N-H str.], M wt. (g/mol) 287.4, C15H19N3OS, HRMS 288(M-1).

TSB_S12- 1-{2-[2-[(4-aminomethylphenyl) methylidene] hydrazin-1-yl]−4-methyl- 1, 3thiazol-5-yl} ethan-1-one: Orange crystal powder, yield= 73%; m.p.= 210℃; UV (*λ*max, 325nm), FTIR (*u*, cm-1)- 739 [C-S-C str.], 1230 [C-O str., (Ar-OCH3) 1310 [C-N str., (R-NR)], 1566 [N=C-H str.(imine)], 1593 [C=C Ar str.], 1635 [C=O str. (thiazole)], 2902 [C-H str.], 3396 [N-H str.], M wt. (g/mol) 302.39; C15H18N4OS, HRMS 301(M-1).

TSB_S13- 1-{2-[2-[(2, 4-dimethoxyphenyl) methylidene] hydrazin-1-yl]−4-methyl- 1, 3thiazol-5-yl} ethan-1-one: Orange crystal powder, yield (97%); m.p. 190℃; UV (*λ*max, 336nm); FTIR (*u*, cm-1)- 732 [C-S-C str.], 1235 [C-O str., (Ar-OCH3)],1575 [C=C Ar str.], 1600 [C=O str. (thiazole)], 1675 [N=C-H str. (imine)], 2850 [C-H str.],2926 [O-H str.], 3348 [N-H str.], M wt. (g/mol) 319.38; C15H17N3O3S, HRMS 320(M+1).

TSB_S14- 1-{2-[2-[(2, 5-dihydroxyphenyl) methylidene] hydrazin-1-yl]−4-methyl- 1, 3thiazol-5-yl} ethan-1-one: Yellow crystal powder, yield (92%); m.p. 70℃; UV (*λ*max, 363nm), FTIR (*u*, cm-1)- 720 [C-S-C str.], 1243 [C-O str., (Ar-OCH3)], 1591[C=O str. (thiazole)], 1591 [C=C Ar str.], 1647 [N=C- H str. (imine)], 2850 [C-H str.], 3300 [Ar-O-H str.],3436 [N-H str.], M wt. (g/mol) 291.34; C13H15N3O3S, HRMS 291(M)+.

TSB_S15- 1-{2-[2-[(2, 5-dimethoxyphenyl) methylidene] hydrazin-1-yl]−4-methyl-1,3thiazol-5-yl}ethan-1-one: Brown crystal powder, yield (68%); m.p. 160℃; UV (*λ*max, 332nm); FTIR (*u*, cm-1)- 743 [C-S-C str.], 1259 [C-O str., (Ar-OCH3)], 1594 [C=O str. (thiazole)], 1610 [C=C Ar str.], 1675 [N=C- H str. (imine)], 2922 [C-H str.], 3436 [N-H str.]; M wt. (g/mol) 319.38; C15H17N3O3S; HRMS 320(M+1).

Designing of Thiazole Schiff Base Derivatives: Fifteen synthesized derivatives which shown good activity *in-vitro* were docked with target in molecular virtual docker (MVD 6.0). The docking process was validated by control docking of reference compound into the active site. The

reference compound in the crystal structures was extracted and docked again to ensure replicability of the orientation and positions in the crystal structure by MVD 6.0. The docking protocol was validated by re-docking the crystallographic ligand; the RMSD between the crystal and docked poses was 1–2 Å. The X-ray crystallography of protein procured from the Protein Data Bank, the results are shown in **Table 1, 2, 3, 4**. Topoisomerase II complex inhibition of *S. aureus* (PDB ID- 2XCT) [17], Peptide deformylase inhibition of *E. coli* (PDB ID- 1BSJ) [18] for antimicrobial activity, Human lanosterol 14*α*-demethylase (CYP51) inhibition (PDB ID- 3LD6) [19] for Antifungal activity, tyrosinase inhibition (PDB ID- 5I38) [20] for antioxidant activity respectively were chosen as a target with the respective interactions and binding pose of topmost compounds shown in **Fig. 3, 4, 5, 6.**

TABLE 1: DOCK SCORE, INTERACTION OF DESIGNED THIAZOLE SCHIFF BASE DERIVATIVES FOR TOPOISOMERASE II COMPLEX INHIBITION (2XCT)

S. No.	Moldock Score	Rerank Score	H-bond score	H-bond Interactions	Substituents at R
1.	-146.227	-91.031	-5.94	His1046,Lys1043,Arg1092	2-hydroxy,5-nitro
2.	-127.535	-88.833	-6.77	Gly1171,Lys1043,Arg1092	5-bromosalicaldehyde
3.	-135.571	-95.588	-7.27	Ser 1173,Asn1166,Asn1170,Tyr1099, Arg1092	2-hydroxy,4-diethylamino
4.	-123.159	-89.977	-3.923	Lys 1043,Arg1092	2-ethoxy
5.	-125.741	-88.536	-13.63	Lys1043,Arg1092,Gly1041,Asn1166,Asn 1170,His1046	2,4-dihydroxy
6.	-123.706	-91.965	-3.318	Lys1043,Arg1092,Ser1085	4-hydroxy,3-methoxy
7.	-129.473	-88.221	-2.168	Lys 1043,Arg1092	3-bromo
8.	-121.162	-93.435	-6.926	Lys1043,Arg1092,Gly1171,Gly1041	4-amino
9.	-131.485	-78.541	-4.236	Lys1043,Arg1092,Asn1166,Gly1171	3-hydroxy,4-methoxy
10.	-130.428	-84.076	-2.284	Ser1085,Arg1092,Tyr1099	4-hydroxy
11.	-128.221	-90.677	-4.739	Lys1043,Arg1092,Ser1173	4-ethyl
12.	-129.143	-93.964	-5.908	Lys 1043, Arg1092	4-aminomethyl
13.	-125.796	-38.137	-2.709	His 1046, Asn1166,Arg1092	2,4-dimethoxy
14.	-132.326	-86.681	-2.348	Lys1043,Arg1092,Ser1085	3,4-dihydroxy
15.	-129.602	-80.444	-3.687	Lys 1043,Arg 1092	2,5-dimethoxy
Ciproflox	-86.007	-11.094	-7.068	Ser1173,Lys1043,Arg1092	-

TABLE 2: DOCK SCORE, INTERACTION OF DESIGNED THIAZOLE SCHIFF BASE DERIVATIVES FOR PEPTIDE DEFORMYLASE INHIBITION (1BSJ)

S. No.	Moldock Score	Rerank Score	H-bond score	H-bond Interactions	Substituents at R
1.	-140.913	-114.204	-7.828	Gly45,Glu133,Arg97	2-hydroxy,5-nitro
2.	-132.364	-106.169	-4.459	Glu95,Ile93,Pro94.Cys90,His132	5-bromosalicaldehyde
3.	-135.104	-86.028	-5.969	Glu95,Cys90,Gly45,Glu133	2-hydroxy,4-diethylamino
4.	-131.968	-98.578	-3.138	Gly45,Glu95,Ile93	2-ethoxy
5.	-131.346	-96.886	-9.368	Glu133, Cys129,Arg97,Gly45	2,4-dihydroxy
6.	-133.854	-110.961	-4.717	Arg97	4-hydroxy,3-methoxy
7.	-125.525	-99.832	-1.333	Glu95,Gln96	3-bromo
8.	-120.368	-89.095	-5.471	Glu95,Arg97, His132,His136	4-amino
9.	-139.041	-115.978	-7.261	Glu133,Cys129,Arg97	3-hydroxy,4-methoxy
10.	-122.987	-100.385	-4.551	Arg97	4-hydroxy
11.	-131.877	-108.551	-0.572	Gln96	4-ethyl
12.	-140.689	-111.057	-4.866	Arg97	4-aminomethyl
13.	-138.132	-115.91	-0.787	Gln96	2,4-dimethoxy
14.	-131.75	-109.337	-7.260	Glu133,Cys129,Arg97	3,4-dihydroxy
15.	-142.01	-117.585	-4.513	Arg97	2,5-dimethoxy
Ciproflo xacin	-140.913	-114.204	-7.828	Gly45,Glu133,Arg97	-

TABLE 3: DOCK SCORE, INTERACTION OF DESIGNED THIAZOLE SCHIFF BASE DERIVATIVES FOR HUMAN LANOSTEROL 14*α*-DEMETHYLASE (CYP51) INHIBITION (3LD6) FOR ANTIFUNGAL ACTIVITY

S. No.	Moldock Score	Rerank Score	H-bond score	H-bond Interactions	Substituents at R
1.	-130.741	-92.789	-5.008	Pro376,Met378	2-hydroxy,5-nitro
2.	-132.122	-91.921	-3.525	Thr318,Trp322,Thr406	5-bromosalicaldehyde
3.	-136.283	-55.251	-5.495	Pro441,cys449	2-hydroxy,4-diethylamino
4.	-129.9	-104.20	-1.767	Thr315	2-ethoxy
5.	-130.454	-79.389	-3.571	Thr318,Thr406,Trp322,Met487,His489, Pro376	2,4-dihydroxy
6.	-135.195	-103.26	-2.877	Leu310,Met378	4-hydroxy,3-methoxy
7.	-131.179	-96.756	-5.532	Thr318	3-bromo
8.	-136.793	-75.673	-5.771	Thr318,His314	4-amino
9.	-130.348	-94.108	-4.970	Thr318,Pro376,His489,Thr406,Trp322	3-hydroxy,4-methoxy
10.	-135.132	-100.99	-4.316	His314,Thr318,His489	4-hydroxy
11.	-134.365	-67.054	-3.613	Trp322,Thr318	4-ethyl
12.	-140.248	-111.84	-3.229	Thr 318,His489,Trp322,Thr406	4-aminomethyl
13.	-131.479	-54.945	-7.021	Thr318,His489	2,4-dimethoxy
14.	-127.997	-80.398	-2.735	Thr318,His489,Trp322,Thr406,Met487	3,4-dihydroxy
15.	-130.741	-92.789	-5.008	Met387,Pro376	2,5-dimethoxy
Keto	-165.948	-108.47	-0.928	Thr315	

Abbreviations: Keto- Ketoconazole.

TABLE 4: DOCK SCORE, INTERACTION OF DESIGNED THIAZOLE SCHIFF BASE DERIVATIVES FOR TYROSINASE INHIBITION (PDB ID- 5I38)

S. No.	Moldock Score	Rerank Score	H-bond score	H-bond Interactions	Substituents at R
1.	-131.758	-77.789	-5.412	Glu 141, Tyr 267, Lys 47, His 41	2-hydroxy,5-nitro
2.	-130.626	-68.526	-3.520	Lys 47, Ala44	5-bromosalicaldehyde
3.	-127.304	-88.587	-4.706	Lys 47, Gly 143	2-hydroxy,4-diethylamino
4.	-124.070	-67.191	-3.375	Lys 47	2-ethoxy
5.	-131.795	-69.613	-9.116	Tyr 267, Ala 44, Lys 47	2,4-dihydroxy
6.	-129.367	-75.005	-5	Lys 47	4-hydroxy,3-methoxy
7.	-135.441	-106.633	-2.065	Lys 47	3-bromo
8.	-145.453	-122.542	-3.125	Lys 47	4-amino
9.	-155.176	-126.766	-3.923	Lys 47, Ala 44	3-hydroxy,4-methoxy
10.	-146.084	-122.598	-5.651	Lys 47, Ala 44	4-hydroxy
11.	-139.570	-67.409	-2.5	Lys 47	4-ethyl
12.	-141.977	-72.521	-4.667	Lys 47	4-aminomethyl
13.	-138.961	-81.173	-2.903	Lys 47	2,4-dimethoxy
14.	-135.531	-67.257	-4.519	Tyr 267, Ala 44,	3,4-dihydroxy
15.	-143.293	-79.053	-3.547	Tyr 267, Ala 44	2,5-dimethoxy
Kojic acid	-74.436	-67.944	-9.075	Gly 216, His 60, His 204, Lys 47, Ala 44, Tyr 267	

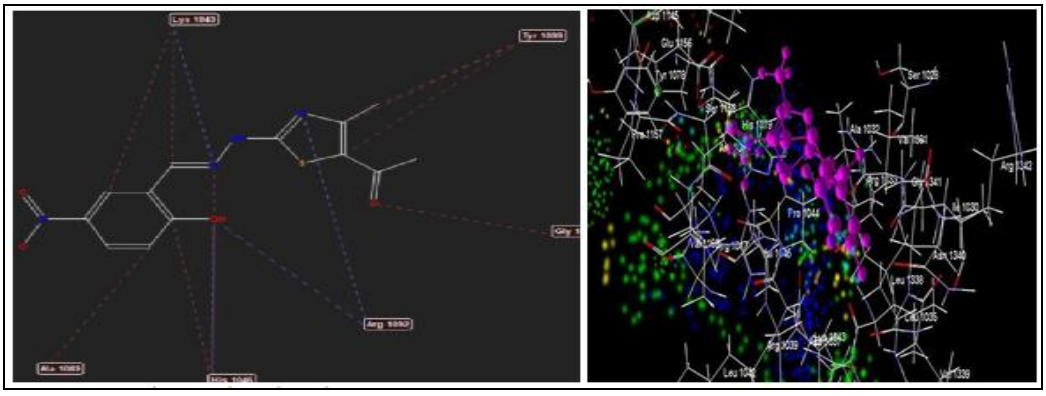


FIG. 3: HYDROGEN BOND AND STERIC INTERACTIONS AND DOCKING POSE OF TSB_S1 FOR TOPOISOMERASE II COMPLEX INHIBITION (2XCT)

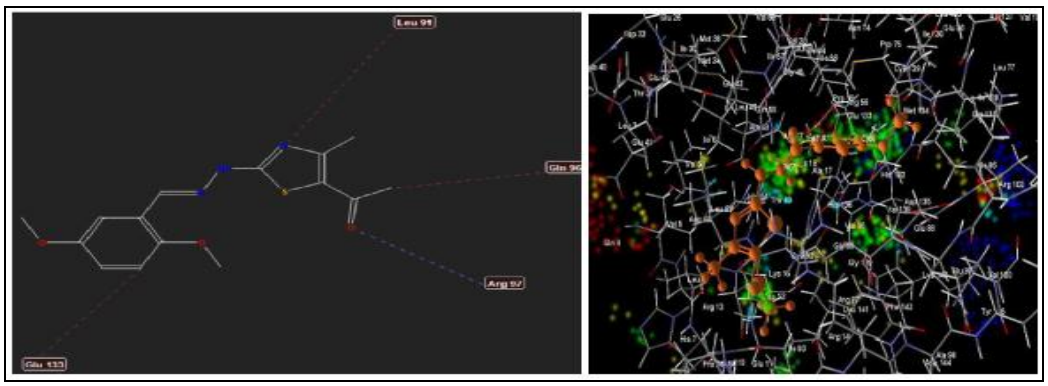


FIG. 4: HYDROGEN BOND AND STERIC INTERACTIONS AND DOCKING POSE OF TSB_S15 FOR PEPTIDE DEFORMYLASE INHIBITION (1BSJ)

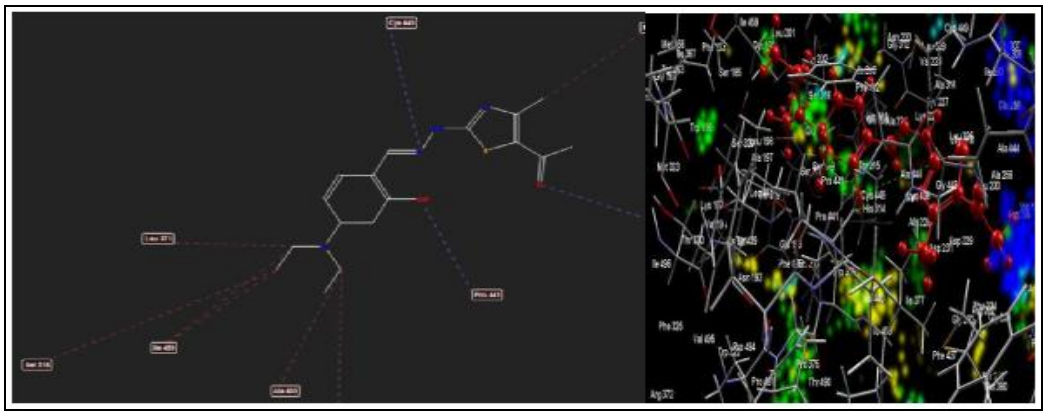


FIG. 5: HYDROGEN BOND AND STERIC INTERACTIONS AND DOCKING POSE OF TSB_S3 FOR HUMAN LANOSTEROL 14ALPHA-DEMETHYLASE (CYP51) INHIBITION (3LD6)

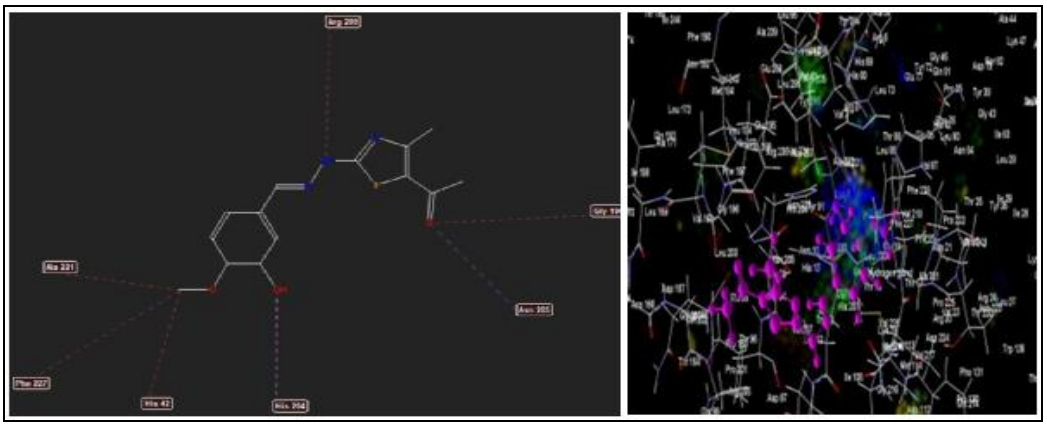


FIG. 6: HYDROGEN BOND AND STERIC INTERACTIONS AND DOCKING POSE OF TSB_S9 FOR INHIBITION OF TYROSINASE ENZYME (5I38)

Antibacterial Assay: The synthesized compounds with good binding interaction in the active sites of PDF of *E. coli* and *S. aureus* were selected for *in-vitro* evaluation. The minimum concentration to inhibit was established using the agar well-plate diffusion method.

Preparation of Samples of Different Concentration: 100, 200, 300 µg/ml of dilutions were prepared in sterile dry test tubes using dimethyl-sulphoxide (DMSO) as solvent. For Antibacterial activity 28 g of agar media was dissolved in 1 litre of autoclaved water heated at 121°C and 15lbs for half an hour. Media was then cooled up to 40-50°C and was poured into a sterilized Petri plate on a levelled horizontal surface to give uniform depth, which was solidified at room temperature in sterilized condition of laminar air flow and nutrient Agar Media was prepared, for Antifungal activity Potato Dextrose Agar Media Suspend 39 g of media was used, then microorganisms were streaked on a culture plate and inhibition Zone was calculated as follows-

Inhibition Zone = Sample diameter / Control/ Standard – diameter of Disc

The standards Ciprofloxacin for antibacterial and Ketoconazole for fungus were prepared in DMSO of 10 µg/ml.

Calculating Percentage Relative Zone Inhibition: The percentage of relative inhibition zone (% RIZ) is calculated as the relative zone inhibition compared to standard at particular concentration by the formula mentioned below- % RIZ = (ZI of sample – ZI of control)/ (ZI of standard – ZI of control) *100 And, RIZ is the percentage of relative zone inhibition and ZI is zone of inhibition (mm).

***In-vitro* Antioxidant Assay:** It was performed on 96 well- micro plate reader -Sigma-Aldrich, model no. MS5608A, were performed at School of Biotechnology, DAVV, Indore. The antioxidant assays conducted *in-vitro* were determined by methods as following four methods.

DPPH Scavenging Assay: This activity measures the antioxidant scavenging activity of compound to reduce free radical. 0.1 ml of 0.24 mg/ml samples and Absorbance at 517 nm was measured after 30 min of incubation in DPPH (0.1 mM) with forceful shaking. Experiment was repeated three times at all the four concentrations, using the given formula-

Activity [% of DPPH reduction] = [(A Ax)/A] × 100

Where, A is absorbance of DPPH in methanol, Ax is absorbance of DPPH by synthesized compounds in methanol. The results of the activity were compared with the kojic acid equivalent antioxidant (KOEA) activity which was calculated as follows-

KOEA= IC_{50} of kojic acid (**µg /ml**)/ IC_{50} of sample (**µ**g /ml)

The higher value of KOEA signifies higher DPPH inhibitory activity [21].

ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) de-colorization Assay: For making ABTS reagent 7mM ABTS stock solution and 245 mM and 2.45 mm of APS (Ammonium persulfate) solution in ultrapure water to form ABTS radical (ABTS•). Incubated for 12–16 h at room temperature and at 734 nm absorbance of ~0.700 was set. various sample solutions at different concentrations were prepared using Phosphate buffer saline (PBS) in eppendorf tubes. The samples were diluted at the desired concentrations of 25, 50, 75, 100 µg/ml. 10 µL of PBS was taken as reference/ zero for the readings, 10 µL of standard of kojic acid, gallic acid along with control and solvent and each sample dilutions were made in separate wells of microplate in triplicate. The wells content was mixed, incubated for 3-5 minutes in dark and read at 734 nm, the decolorization effect caused by each samples/standard relative to the absorbance of the control was calculate in DPPH activity.

FRAP Assay: 2, 4, 6- tri [2-pyridyl]-s-triazine, $FeCl_3.6H_2O$, Acetate buffer were mixed with Iron (II) sulfate heptahydrate ($FeSO_4.7H_2O$), 3ml of the above solution was taken and samples were added and the solution was mixed with pipette tip to homogenize the contents filled in Eppendorf tubes which was incubated at 37°C for 15 min. Samples were run by conventional 96- well microplate reader. Each well was properly marked before pipetting for sample identification, then 250 µl of the content was transferred into the corresponding well and the absorbance was determined at 593 nm. Requirements- These solutions should be prepared only on the day of assay; the container should be wrapped in aluminium foil and the solutions be kept on ice. The test was performed twice and air bubble should be pricked to avoid any bias in analysis of readings [22].

Hydrogen Peroxide (H_2O_2) Scavenging Assay: Hydrogen peroxide (40 mM) prepared in phosphate buffer (pH 7.4) and 100 µg/mL of distilled water were added. Absorbance of hydrogen peroxide at 230 nm was determined 10 minutes later against a blank as phosphate buffer. The percentage of H_2O_2 scavenging was calculated by UV visible spectrophotometer.

Generalized Formula for FRAP Values and H_2O_2 Values Calculation: 10 FRAP/ H_2O_2 Value for Sample (µM) = Sample Absorbance * FRAP/ H_2O_2 Value of Standard (µM) /Absorbance by Standard.

RESULTS AND DISCUSSION:

Docking Analysis: Fifteen thiazole Schiff base derivatives were synthesized and docked for antimicrobial activity against topoisomerase II

complex inhibition (PDB ID- 2XCT) compound-1 (having 2-hydroxy, 5-nitro group at R position) shown highest dock score and strong hydrogen bond interaction with His 1046, Lys 1043, Arg 1092 with topoisomerase II and In *E. coli* peptide deformylase (PDB ID- 1BSJ) the compound-TSB_S15 (having 2,5 di-methoxy group at R position) showed a highest moldock score among all compounds, more than ciprofloxacin. Most active compound-15 showed interaction with catalytic site residues Gly 45, Glu 133, Arg 97 in the enzyme peptide deformylase. For Antifungal activity Human lanosterol 14alpha-demethylase (CYP51) inhibition (PDB ID- 3LD6) compound-3 (having 2-hydroxy, 4-diethyl amino group at R position) has the highest dock score and strong hydrogen bond interaction with the amino acid Pro 441, Cys 449, For Antioxidant activity inhibition of tyrosinase enzyme (PDB ID- 5I38) the compound TSB_S9 (having 3-hydroxy, 4-methoxyphenyl substitution at R position) has the maximum dock score in series exhibit hydrogen-bond interactions as Lys 47, Ala 44.

Antibacterial, Antifungal Activity: Total 15 synthesized compounds tested for strains of *S. aureus, M. luteus, P. vulgaris* and *E. coli* for their antibacterial activity and for antifungal activity *A. niger* and *C. albicans* were taken and zone of inhibition was measured and with this percent inhibition was determined with respect to standard. Zone of inhibition, Percentage Relative inhibition zone diameter of synthesized Statistical analyses were performed using GraphPad Prism 9.0. Data are presented as mean ± SD. Comparisons were made using one-way ANOVA followed by Tukey's post hoc test; $p < 0.05$ considered significant**.**

TABLE 5: ZONE OF INHIBITION OF SYNTHESIZED THIAZOLE SCHIFF BASE DERIVATIVES FOR ANTI BACTERIAL AND ANTI- FUNGAL ACTIVITY

Comp. ID	Zone of inhibition (in mm)											
	S. aureus		*M. luteus*		*P. vulgar is*		*E. coli*		*A. niger*		*C. albicans*	
Conc. µg/ml	200	300	200	300	200	300	200	300	200	300	200	300
TSB_S1	12	26	3.7	8.2	12.5	32.5	15.5	28	1.2	5	6	15.3
TSB_S2	5	9.1	1.7	5.2	10	18	5	10.2		26	17	30.5
TSB_S3	-	-	17	25	1.7	9	3	8	12	23	13	23.5
TSB_S4	1.9	4.5	3.1	9.7	5	12	-	-	15	8	13	23.5
TSB_S5	5	11.2	10.6	19.2	2.5	9	2	6.3	2.3	7	-	-
TSB_S6	7	12.4	8.5	15	9	15	-	-	3	6.2	5	12.4
TSB_S7	8	19.5	17.5	25	10	19	6	12	19	25	-	-
TSB_S8	4	9.2	7	11.8	-	-	3.5	8.2	2.5	6	2	8.6
TSB_S9	-	-	14	28	8	13.5	16	29	15	35.4	-	-
TSB_S10	6.2	10	19	30	16	27	2.5	9	4	9.3	5	11.4
TSB_S11	12	28	7	16	5	12	5	12	-	-	19	30
TSB_S12	3	8.5	3.2	9	-	-	15	23	2.8	5.2	6	10.8
TSB_S13	5.1	10	-	-	-	-	-	-	-	-	12.5	22.5
TSB_S14	4.2	22	6	12	3	9	14	23	5	9.8	-	-
TSB_S15	3.2	7.9	-	-	9	25	17	25.5	5	10.2	3	8
Ciprofloxa cin	42	53	42	53	43	55	41	52				
Ketoconaz ole									45	53	42	55

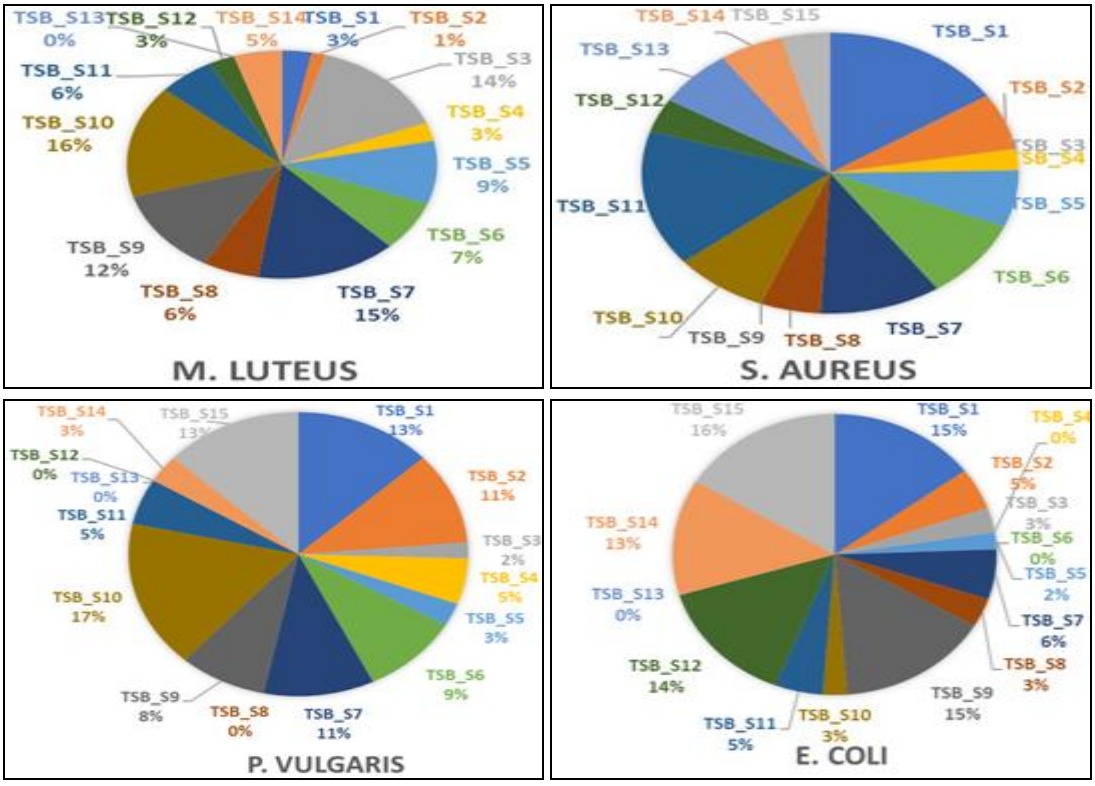
TABLE 6: PERCENTAGE RELATIVE INHIBITION ZONE DIAMETER OF SYNTHESIZED THIAZOLE SCHIFF BASE DERIVATIVES FOR ANTI-BACTERIAL AND ANTI- FUNGAL ACTIVITY

Comp. ID												**C. *albicans***
Conc.	*S. aureus*		*M. luteus*		*P. vulgaris*		*E. coli*		**A. *niger***			
	200	**300**	**200**	**300**	**200**	**300**	**200**	**300**	**200**	**300**	**200**	**300**
TSB_S1	28.6	49.1	8.2	15.5	29.1	59.1	37.8	53.8	2.7	9.1	13.3	27.8
TSB_S2	11.9	17.2	3.8	9.8	23.3	32.7	12.2	19.6	26.7	47.3	37.8	55.5

TSB_S3	-	-	38.4	47.2	4.0	16.4	7.3	15.4	33.3	41.8	28.9	42.7
TSB_S4	4.5	8.5	6.9	18.3	11.6	21.8	-	-	6.7	14.5	28.9	42
TSB_S5	11.9	21.1	23.6	36.2	5.8	15.4	4.9	12.1	5.1	12.7	5	12.3
TSB_S6	16.7	23.4	18.9	28.3	20.9	27.3	-	-	6.7	11.3	11.1	22.5
TSB_S7	19.0	36.8	38.9	47.7	23.3	34.5	14.6	23.1	42.2	45.5	4.3	14.7
TSB_S8	9.5	17.4	15.6	22.3	-	-	8.5	15.8	5.6	10.9	4.4	15.6
TSB_S9	-	-	31.8	53.4	18.6	24.5	39.0	55.8	33.3	64.4	-	-
TSB_S10	14.8	18.7	42.2	57.5	37.2	49.1	6.1	17.3	8.9	16.9	11.1	20.7
TSB_S11	28.6	52.8	15.6	30.2	11.6	22	12.2	23.1	-	-	42.2	54.5
TSB_S12	7.1	16.0	7.1	17.0	-	-	36.6	44.2	6.2	9.5	13.3	19.6
TSB_S13	12.1	18.9	-	-	-	-	-	-	2.7	9.1	27.8	40.9
TSB_S14	15.0	41.5	13.3	22.6	7.0	16	34.1	44.2	26.7	47.3	-	-
TSB_S15	7.6	14.9	-	-	29.1	45.5	41.5	49.0	33.3	41.8	6.7	14.5
Ciprofloxacin	42	53	42	53	43	55	41	52				
Ketoconazole									45	53	42	55

TABLE 7: IC_{50} VALUES OF SYNTHESIZED THIAZOLE SCHIFF BASE DERIVATIVES FOR ANTI-BACTERIAL (GRAM POSITIVE, GRAM NEGATIVE), ANTI- FUNGAL ACTIVITY

		IC_{50}(µg/ml)															
Sp. Of Bacteria	**Conc. (µg/ml)**	**TSB_S1**	**TSB_S2**	**TSB_S3**	**TSB_S4**	**TSB_S5**	**TSB_S6**	**TSB_S7**	**TSB_S8**	**TSB_S9**	**TSB_S10**	**TSB_S11**	**TSB_S12**	**TSB_S13**	**TSB_S14**	**TSB_S15**	**STD.**
S. aureus	200																
	300	322	866									307					268
M. luteus	200	103	168														
	300	3	3	309		422		300		294							268
P. vulgaris	200																
	300	276	457				537									337	259
E. coli	200							319									
	300	274								268					325	284	273
A. niger	200	198															
	300	4	378	359						253					337	344	255
C. albicans	200																
	300	603	272	375	353							265		368			255



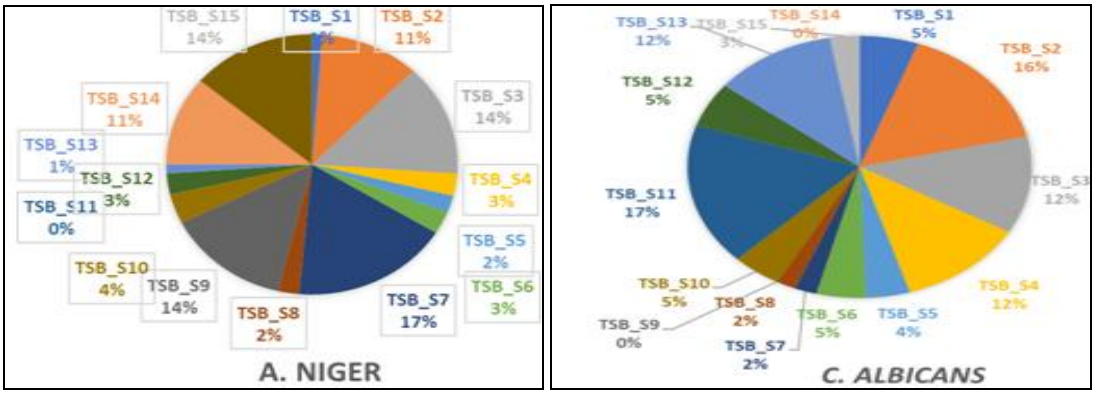


FIG. 7: PERCENTAGE RELATIVE INHIBITION ZONE DIAMETER OF SYNTHESIZED THIAZOLE SCHIFF BASE DERIVATIVES FOR ANTI-BACTERIAL AND ANTI- FUNGAL ACTIVITY

For Gram-positive Bacterial Activity: In *S. aureus*- TSB_S1, TSB_S7, TSB_S11, TSB_S14 displayed moderate inhibition as compared to standard drug ciprofloxacin and TSB_S8 displayed poor inhibitory activity at 300 µg/ml concentration **Table 7** and in *M. luteus*- TSB_S3, TSB_S7, TSB_S9, TSB_S10, TSB_S11 showed good inhibitory activity whereas TSB_S13 shown poor inhibitory activity at 300 µg/ml concentration.

For Gram-negative Bacterial Activity: In *P. vulgaris*- Effective Percentage Relative inhibition zone was shown by TSB_S1, TSB_S9, TSB_S10, TSB_S15 showed good inhibitory activity and in E. coli- TSB_S1, TSB_S7, TSB_S9, TSB_S10, TSB_S14 showed good inhibitory activity.

For Antifungal Activity: In *A. niger* TSB_S2, TSB_S3, TSB_S7, TSB_S9 shown good activity and in *C. albicans* TSB_S2, TSB_S3, TSB_S11, TSB_S13 shown effective percentage relative zone of inhibition as shown in **Fig. 7.** The correlation between these two studies for the above designed and synthesized compounds exhibited that in *in-silico* studies of antibacterial activity (2XCT) the compounds TSB_S1, TSB_S3, TSB_S7, TSB_S13 showed good results in *in-silico* studies and compounds TSB_S1, TSB_S7, TSB_S11, TSB_S14 showed good results *in-vitro* in *S. aureus* whereas in *M. luteus* TSB_S3, TSB_S7, TSB_S9, TSB_S10, TSB_S11 exhibited good results *in vitro* which were similar to the compounds *in-silico* studies. For gram negative bacteria (1BSJ) for *In-silico* studies TSB_S1, TSB_S9, TSB_S12, TSB_S15 indicated good results whereas in *in-vitro* activity for *P. vulgaris* TSB_S1, TSB_S9, TSB_S10, TSB_S15, whereas for *E. coli* the results of in vitro activity were showed by compounds TSB_S1, TSB_S7, TSB_S9, TSB_S10, TSB_S14 which were similar to that obtained by docking studies. The compounds TSB_S3, TSB_S7, TSB_S9, TSB_S13 showed good results in *In-silico* studies and compounds TSB_S2, TSB_S3, TSB_S7, TSB_S9 showed good antifungal activity *in-vitro* in *A. niger* and TSB_S2, TSB_S3, TSB_S11, TSB_S13 showed good activity in *C. albicans*. Microbiological evaluation revealed good activity against Gram- positive bacteria (*M. luteus*), Whereas inhibition of *E. coli* in Gram-negative bacteria was more than *P. vulgaris* and *C. albicans* showed better antifungal activity than *A. niger*. More active bacterial and fungal inhibition found by Microbiological evaluation- Gram-positive bacterial activity was more efficient than Gram-negative bacterial activity and descending order of inhibition against strains is shown below- *M. luteus> S. aureus; E. coli> P. vulgaris; C. albicans > A. niger*.

DPPH Scavenging Assay: It's distinguished by the donation of hydrogen by the synthesized compound to the DPPH molecule. All the synthesized compounds showed good DPPH inhibition activities with IC_{50} value of 14 µg/ml TSB_S7 as minimum and best compound whereas TSB_S11 was found to be least effective with very high IC_{50} value of 157 µg/ml. Compound TSB_S8 and TSB_S14 were also found to be potent. The compound shown good activities via amino, hydroxyl, ethoxy group. Activity in the ascending order is shown below: TSB_S7 > TSB_S8 > TSB_S14 > TSB_S15 > TSB_S13 > TSB_S10 > TSB_S9 > TSB_S6 > TSB_S5 > TSB_S4 > TSB_S1 > TSB_S3 > TSB_S2 > TSB_S12 > TSB_S11.

ABTS Radical Scavenging Assay: It's the donation of hydrogen by the synthesized compound to the ABTS molecule. All the synthesized compounds showed good radical scavenging activities with IC_{50} value of 53 µg/ml TSB_S14 as minimum and best compound whereas TSB_S12 was found to be least effective with very high IC_{50} value of 113 µg/ml. Compound TSB_D15 and TSB_D13 were also found to be potent. The compound shows good activities due to the presence of hydroxy and methoxy di substitution, and substituted 4-aminomethyl group. The other synthesized compounds also showed good scavenging activity. The activity in the ascending order is shown below: 14 15 TSB_S14 > TSB_S15 > TSB_S13 > TSB_S10 > TSB_S8 > TSB_S9 > TSB_S6 > TSB_S5 > TSB_S4 > TSB_S7 > TSB_S1 > TSB_S3 > TSB_S2 > TSB_S12 > TSB_S11.

FRAP Reducing Power Assay: Some compounds showed worthy scavenging activity while other compounds showed reasonable activity. All compounds displayed scavenging activities with IC_{50} value of 13 µg/ml, TSB_S14 as minimum and best compound whereas TSB_S1 was found to be least effective with very high IC_{50} value of 169 µg/ml **Fig. 8**.

Compound TSB_D15 and TSB_D8 were also found to be more potent. The compound shows good activities due to the presence of di-hydroxy, di-methoxy. The activity in the ascending order is shown below: TSB_S14 > TSB_S15 > TSB_S8 > TSB_S10 > TSB_S13 > TSB_S9 > TSB_S6 > TSB_S12 > TSB_S4 > TSB_S7 > TSB_S1 > TSB_S3 > TSB_S2 > TSB_S5 > TSB_S11.

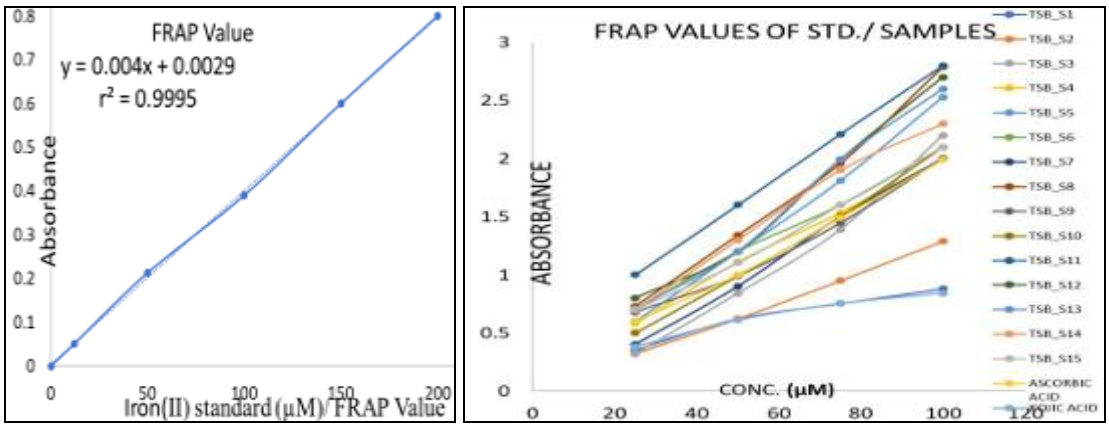


FIG. 8: GRAPH SHOWING IRON (II) STANDARD (µM)/ FRAP VALUE PLOTTED AGAINST ABSORBANCE

Hydrogen Peroxide (H_2O_2) Scavenging Assay: Compound TSB_S15 and TSB_S13 showed good scavenging activity with IC_{50} value between 41 µg/ml and 101 µg/ml. The compound shows good activities due to the presence of di hydroxy and di-methoxy substitution. The activity in the ascending order is shown below: TSB_S14 > TSB_S15 > TSB_S13 > TSB_S10 > TSB_S8 > TSB_S9 > TSB_S6 > TSB_S5 > TSB_S4 > TSB_S7 > TSB_S1 > TSB_S2 > TSB_S3 > TSB_S12 > TSB_S11.

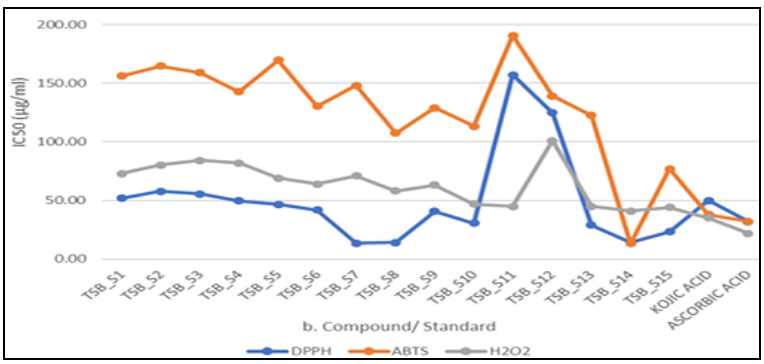


FIG. 9: GRAPH SHOWING COMPARISON OF IC_{50} (MG/ML) OF DPPH, ABTS, HYDROGEN PEROXIDE (H_2O_2) SCAVENGING ASSAY

TABLE 8: IC_{50} (µg/ml) OF DPPH, ABTS, FRAP, HYDROGEN PEROXIDE (H_2O_2) SCAVENGING ASSAY

Comp. ID	IC_{50}(µg/ml)			
	DPPH	ABTS	FRAP (µM)	H_2O_2
TSB_S1	51.78±2.14	85.06±1.53	156.1±1.01	73.06±1.13
TSB_S2	57.93±1.49	96.12±2.00	164.63±0.421	80.12±1.20
TSB_S3	55.68±1.08	92.31±3.00	159.02±0.21	84.31±1.7
TSB_S4	49.62±5.99	83.33±3.21	142.68±1.43	82.33±1.21
TSB_S5	46.59±1.50	81.07±1.53	169.63±.74	69.07±0.53
TSB_S6	41.88±1.12	76.16±2.00	130.49±0.34	64.16±0.70
TSB_S7	13.59±0.73	83.76±1.00	148.17±0.11	71.76±0.90
TSB_S8	13.95± 1.55	70.43±1.00	107.32±0.43	58.43±0.230
TSB_S9	40.70±4.13	75.82±1.51	129.15±0.65	63.82±0.41
TSB_S10	30.47±2.30	59.68±1.00	113.41±0.34	47.68±1.09
TSB_S11	157.06±1.52	57.70±1.21	190.73±0.76	45.70±1.21
TSB_S12	124.80±2.57	113.80±2.0	139.02±0.78	101.80±0.50
TSB_S13	28.86±1.45	57.70±1.79	122.56±0.98	45.70±1.79
TSB_S14	14.34±1.02	53.64±2.00	13.29±1.76	41.64±2.00
TSB_S15	23.43±1.32	56.65±2.61	76.89±1.8	44.65±2.61
Gallic acid	50±1.45	38±1.08	26.27±2.9	35±1.08
Kojic acid	18±2.10	32±1.00	70.18±1.42	22±1.00

TSB_S7, TSB_S8, TSB_S10, TSB_S14, TSB_S15 gave the best results with highest dock scores and interactions and these compounds also showed best results in *in-vitro* antioxidant activity Graph showing comparison of IC_{50} (µg/ml) in **Fig. 9, Table 8** showing IC_{50} (µg/ml) of DPPH, ABTS, FRAP, Hydrogen peroxide (H_2O_2) scavenging assay. The compounds TSB_S7, TSB_S8, TSB_S14, TSB_S15 showed best results for *in-vitro* 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. In ABTS assay and Hydrogen peroxide assay compounds TSB_S14, TSB_S15, TSB_S13, TSB_S10 showed good activity whereas in FRAP reducing power assay compounds TSB_S14, TSB_S15, TSB_S8, TSB_S10 gave good results and TSB_S9 gave moderate results in *in-silico* activities. These compounds showed good to moderate activity in all the *in-vitro* antioxidant methods, due to the presence of electron donating group at ortho and para position increases the potency respectively.

CONCLUSION: In this research work molecular docking for the designing of Thiazole Schiff base derivatives. The results of docking study comply with the results of *in-vitro* evaluation of the antimicrobial and antioxidant study. Compounds TSB_S1, TSB_S3, TSB_S9, and TSB_S15 showed promising antimicrobial activity along with compound TSB_S14 for antioxidant activity. Among all synthesized compounds TSB_S14 holding small hydrophobic fluoro group on R position of ring B while electron withdrawing nitro group on R3 position of ring C found to be most active. The above synthesized compounds which showed best results in *in-vitro* and in *in-silico* studies can further be evaluated for *in-vivo* future activity and further toxicity studies can be performed.

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