



Antibacterial activity of the root extracts of *Garcinia Kola* against MDR *Staphylococcus aureus*: an *Invitro* and *in silico* studies**Abdulbasit Haliru YAKUBU¹, Hassan Braimah YESUFU¹, Muhammad Mustapha MUHAMMAD² and Amina Jega YUSUF³**¹*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, P.M.B. 1069, University of Maiduguri, Maiduguri, Borno, Nigeria.*²*Department of Microbiology, Faculty of Science, PMB 1069, University of Maiduguri, Maiduguri, Borno, Nigeria.*³*Department of Pharmaceutical and Medicinal Chemistry, Faculty of Sciences, Usmanu Danfodiyo University, P.M.B. 2346, Sokoto, Nigeria*Corresponding author mail: pharmahy071@gmail.com

Abstract

Multi Drug Resistance (MDR) *Staphylococcus aureus* is an important bacteria with clinical and economic implications. Plants including *Garcinia kola* provides bioactive principles with diverse structural and biological features. The *n*-butanol fraction of *G. kola* root extract recorded the highest activity against MDR staph aureus (18.50 ± 0.41) compared to the chloroform (10.00 ± 2.12) and methanol (8.16 ± 0.62) extract, with no activity recorded with the *n*-hexane extract. Analysis of the *n*-butanol fraction on GC-MS recorded 14 phytoconstituents with varying structural composition; containing important scaffolds & motifs of benzoquinone, imidazo[1,2-*a*] pyridine, Chlorocarbazole and azetidine that present key pharmaceuticals as antibiotic for drug development. Further *insilico* molecular docking studies of these compounds on antibacterial drug target; Tyrosyl-tRNA synthetase (PDB 1JJJ) from MDR staph aureus was documented. Nine (9) compounds had good binding scores ranging from -4.63 to -7.08 kcal/mol; with 3,8-di-*tert*-butyl-5,6-diphenyl-2,9-dithia-1-phosphabicyclo[4.3.0]nona-3,7-diene 1-sulfide having the highest score. The compounds formed various bonding with the 1JJJ amino acid residues including H-bond, van der waal and π interactions. (S)-(-)-2-Azetidinecarboxylic acid and 2-Hydroxyethyl benzoate bind to the most active binding pocket (Drug score: 0.82 & 0.72) while 9,9-dichloro-9-silafluorene tend to bind outside the active binding pocket. They also have good pharmacokinetic and toxicity profile. As a result of satisfactory *in vitro* and *in silico* experimental validation, these compounds are regarded as promising potential antibiotics against MDR *Staphylococcus aureus*.

Keywords: *Garcinia kola*, Antibacterial, MDR *Staphylococcus aureus*, tyrosyl-tRNA synthetase (YRS), Molecular docking.

Introduction

In the past decades, there had been an alarming increase in the rise of antimicrobial

resistance; this translates a serious public health concern as choice of clinical drugs become limited and ineffective which in

turn, results to negative clinical and economic consequences on patient's health, increase in nosocomial infection, prolonged hospital stay and mortality. The mortality due to this infections is projected to be over a 10 million by 2050 (Ferdes, 2018). Thus, a prompt call for global advocacy campaign in antibiotic stewardship.

Among the common encountered bacteria of clinical importance is *Staphylococcus aureus* which is the most common cause of nosocomial infections, bacteremia and is a bacterial pathogen with high propensity to develop antibiotic resistance (Steinig *et al.*, 2019; Kot *et al.*, 2020). The methicillin resistance *Staph. aureus* (MRSA) confers its resistance to β -lactam antibiotic by acquiring the genetic element; *Staphylococcal* cassette chromosome *mec*, which carries the *mecA* gene and also that of the new variant *mec C* (Kot *et al.*, 2020). This MRSA later become resistant to other class of antibiotic including broad spectrums by acquiring new antimicrobial resistance elements and are termed Multi-drug Resistant (MDR) MRSA (Kot *et al.*, 2020). Hiramatsu and colleagues described the genetic basis of the ability of *Staph. aureus* to acquire multi-antibiotic resistance (Hiramatsu *et al.*, 2014). MDR MRSA presents serious challenges in the treatment and control of *Staph. aureus* infections; standard clinical agents used in its treatment include vancomycin, linezolid, daptomycin, tigecycline, telavancin, and ceftaroline (Anstead *et al.*, 2013; Kot *et al.*, 2020).

Aminoacyl-tRNA synthetases (AARSs) are key important enzyme that are involved in bacterial transcription, translation and signaling pathways. They catalyse the covalent binding of relevant amino acid with specific tRNA. Tyrosyl-tRNA synthetase (TyrRS) is a class I synthetases and because

of their role in protein synthesis, inhibitors of this enzymes are being explored for the discovery and development of potential new antibiotic agents (Farshadfar *et al.*, 2020)

Plant phytochemicals have been explored and documented for their potential antibacterial activity against sensitive and resistant pathogens (Khameneh *et al.*, 2019).

A review of its ethnobotanical, phytochemistry, pharmacological & toxicological, and therapeutic properties of *G. kola* have been documented (Bubu *et al.*, 2016; Tcheghebe *et al.*, 2016). A plethora of literature's emerged on the antibacterial activity of *G. kola* especially the seed and leave part. However, there's scarcity of research work on the antibacterial activity of the root part of *G. kola* against MDR *staph aureus*.

With the increase in antibiotic resistance and limited availability of new drug entry for possible clinical use against MDR *staph aureus*, it's imperative for the research on new bioactive principles against this organism. In this study, we undertook the antibacterial studies of the root extracts (n-hexane, n-Butanol, chloroform, and methanol) of *G. kola* against isolated MDR *Staph. aureus*, as well as carried out *in silico* molecular docking and ADME/Toxicity analysis of the phytoconstituents from the active extract against Tyrosyl-tRNA synthetase.

Materials and method.

Plant Collection and Identification

Fresh root parts of *G. kola* were collected aseptically in October 2022 from Jos LGA, Plateau State, Nigeria, and it was identified by a Medicinal Botanist (Mr. Namadi Sanusi) of the Biology department, ABU

Zaria, Nigeria by comparing with voucher specimen number; ABU0297. The roots were washed with water to remove external impurities, shade-dried under shade and pulverized into powder prior to extraction.

Preparation of Plant Extract and Fractions

The method reported by Yakubu *et al.*, (2020) was adopted with modification. In this study, 500 g of the pulverized root sample material was extracted using maceration method with n-hexane, chloroform, n-butanol and methanol and allowed for 72 h under room condition. The mixture was filtered with a filter paper and allowed to dry under room temperature to obtain the crude extracts each; stored in a desiccator and used for further analysis.

Antimicrobial Assay Test Organisms

Isolates of *MDR staphylococcus aureus* were obtained from the Microbiology department, University of Maiduguri and were stored at 2 – 8 °C until required.

Preparation of extract solutions and test organism for Pathogenic Assay The method of Yakubu *et al.*, (2020) was adopted; a stock solution of 1000 mg/mL was prepared and a two-fold serial dilution was carried out to obtain working solutions of varying concentrations. Test organisms cultured for 24hrs were suspended in a sterile bottle containing pure broth. Normal saline was added gradually and the turbidity was observed and compared to that of 0.5 McFarland standard; this was then diluted to produce 10⁶cells/mL and used in the experiments.

Nutrient agar was prepared accurately to the manufacturer's specification and sterilized at

121 °C for 15 min which was then allowed to cool to 50 °C in a water-bath. The test organism (1 mL containing 10⁶ cells/mL) was inoculated into pre-labeled petri plates (90 mm diameter), then 19 mL of the molten agar was added to each petri plate, shaken and allowed to set at room temperature on a flat surface (Yakubu *et al.*, 2020).

Antimicrobial Susceptibility Assay – agar well diffusion method

The antibacterial activity of the crude extracts was determined in accordance with the agar-well diffusion method described by Indabawa and Arzai (2011) and Yakubu *et al.*, (2020). The bacterial isolates were grown for 18 h in a nutrient broth and standardized to 0.5 McFarland standards (10⁶ cfu/mL). Two hundred microliter (200 µL) of the standardized cell suspensions were spread on a Mueller-Hinton agar and wells were bored into the agar using a sterile 6 mm diameter cork-borer. Approximately 100 µL of the crude extract at 100, 75, 50 and 25 mg/mL were introduced into the wells, allowed to stand at room temperature for about 2 h and then incubated at 37 °C. Controls were set up in parallel using the solvents that were used to reconstitute the extract. After 24 h, the plates were observed for the zones of inhibition. The effects were compared with those of Vancomycin at a concentration of 5 mg/mL. Antibacterial activity was evaluated by measuring the diameters of zones of growth inhibition in triplicates and results were presented as Mean±SEM. 00 indicates negative and no effect, diameter < 8.0 mm zone of inhibition indicates low activity, >8 mm of inhibition indicates high activity (Indabawa and Arzai, 2011).

GC-MS Analysis

The method of GC-MS analysis employed by Osuntokun and colleagues was adopted. A GC clarus 500 Perkin Elmer system comprising a AOC-20i auto sampler and gas chromatograph interfaced to a mass spectrometer instrument was employed for the Gas column- Mass spectroscopy; operating with a column elite-1 fused silica capillary column (30x0.25 mm IDx1EM df, composed of 100 % dimethyl polysiloxane), electron impact mode at 70 eV; helium (99-999 %) was used as carrier gas at a constant flow of 1 ml/min and an injection volume of 0.5 EI.

Preparation of protein complex

The 3D structure of the protein target *staph. aureus* tyrosyl-tRNA synthatase PDB 1JJJ was retrieved from the protein data bank PDB (Pisano *et al.*, 2019). Missing loops were checked for, alternate conformations were removed, bond orders were determined, side chains were optimized and fixed, improper chirality was identified, disulfide bonds were checked, steric clashes were identified and fixed, protonation states were determined, and the protein were optimized and their energy calculated using a program implemented in SwissPDBViewer (v4.1.0) (Khare *et al.*, 2022).

Molecular Docking

The most critical requirement for interaction of tyrosyl-tRNA synthatase with the ligands

it's the proper orientation and conformation of the ligands in its active sites. Compounds from GC-MS with desirable physicochemical properties were selected and ligands 3D structure were obtained from PubChem. The molecular docking was analysed with AutoDock4.0. The docking analysis was evaluated at a free binding energy of the protein- ligand complex determined with a total of 110 runs, maximum evaluation of 2500,000, maximum generation of 27,000 and with a population size of 150. The dimension of the grid was set at 60x60x60 Å with a grid spacing of 0.375 Å. A Lamarckian Genetic Algorithm (LGA) was used to compute the free binding energy while Ligplot+v.1.4.5 tool was utilized to investigate the molecular interactions of the chemicals with the target protein (Gurung *et al.*, 2022), and Pymol Molecular Graphics System, Version 1.8 Schrodinger, LLC (DeLano, 2002) and Discovery studio. Prediction of binding site and 2D ligand-protein complex interaction was viewed with DoG Site Scorer and Poseview respectively from ProteinsPlus sever (Volkamer *et al.*, 2012 and Fährrolfes *et al.*, 2017).

Drug Likeness and Pharmacokinetics Analysis

All docked ligands were screened for the Lipinki's rule of five (RO5), pharmacokinetics and toxicity profile (ADME/TOX) using the Swiss ADME (Daina *et al.*, 2017) and Data Warrior tool (Sander *et al.*, 2015).

Results**Table 1:** *In vitro* antimicrobial activity of *G. kola* extracts on *MDR staph. Aureus*

Concentration (mg/ml)	Extract/ Zone of Inhibition				
	n-Hex	CHCl ₃	n-But	MeOH	Van(5mg/mL)
100	00.00±0.00	10.00±2.12	18.50±0.41	8.166±0.62	25.00±1.30
75	00.00±0.00	8.83±1.50	13.50±0.40	8.16±0.23	-
50	00.00±0.00	7.50±0.93	11.83±0.85	3.33±0.24	-
25	00.00±0.00	6.33±1.40	11.16±0.62	3.00±0.35	-

Data was expressed as mean±SEM

Key: n-Hex =n-hexane; CHCl₃ = chloroform; n-But: n-Butanol; MeOH: methanol; Van: Vancomycin

Table2: GC-MS analysis of the n-Butanol crude extract of *G. kola*

S/N	Pub Chem ID	Compound	Formula	Molecular Weight	Retention Time (min)	Peaks
1	CID_619544	2-Hydroxy-3-(thiophen-2-yl)methyl-5-methoxy-1,4-benzoquinone	C ₁₂ H ₁₀ O ₄ S	250	4.02	0
2	CID_619583	9,9-Dichloro-9-silafluorene	C ₁₂ H ₈ Cl ₂ Si	250	7.310	0
3	CID_5732	Zolpidem	C ₁₉ H ₂₁ N ₃ O	307	7.310	0
4	CID_616643	Pyridazine-3,5-dicarbonitrile, 1,6-dihydro-4-amino-6-imino-1-(2-nitrophenyl)-	C ₁₂ H ₇ N ₇ O ₂	281	7.310	0
5	CID_240576	Pyrimidine, 5-bromo-2,4-bis(methylthio)-	C ₆ H ₇ BrN ₂ S ₂	250	2.956	1

6	CID_62 2021	5H-Naphtho[1,8- bc]thiophen-5- one, 3,4- dihydro-2-phenyl-	C17H12OS	264	7.42	2
7	CID_61 6496	9,9'-Bis(3,6- dichlorocarbazole)	C24H12Cl4N2	468	7.42	2
8	CID_59 0350	3,8-Di-t-butyl-5,6- diphenyl-2,9- dithia-1- phosphabicyclo[4.3.0]nona -3,7- diene 1-sulfide	C26H31PS3	470	7.42	2
9	CID_65 86	Methyl chloroformate	C2H3ClO2	94	1.708	1
10	CID_24 9920302	Diborane(6), μ -mercapto-	B2H6S	60	1.909	2
11	CID_13 770	1- Methylcyclopropanemetha nol	C5H10O	86	1.909	2
12	CID_16 486	(S)-(-)-2- Azetidinecarboxlic acid	C4H7NO2	101	2.55	1
13	CID_79 83	Butanoic acid, butyl ester	C8H16O2	144	3.534	2
14	CID_66 747	2-Hydroxyethyl benzoate	C9H10O3	166	3.534	2

Table 3: Physiochemical analysis of constituents from the n-Butanol crude extract of *G. kola*

S/N	PubChem ID	Molecular weight(≤ 500)	Number of HBA (≤ 10)	Number of HBD (≤ 5)	MolLogP (≤ 5)	Druglikeness
1	CID_619544	250.273	4	1	1.2614	3.7229
2	CID_619583	251.88	0	0	2.7656	-37.314
3	CID_5732	307.396	4	0	2.7975	3.3181
4	CID_616643	281.235	9	2	-0.8212	-6.832
5	CID_240576	251.172	2	0	2.1155	-3.2172
6	CID_622021	264.347	1	0	4.6609	-0.10276
7	CID_616496	470.185	2	0	7.7372	0.95217
8	CID_590350	470.704	0	0	9.3002	-9.1649
9	CID_6586	94.4968	2	0	0.8196	-12.134
10	CID_24992030 2	-	-	-	-	-
11	CID_13770	86.1334	1	1	0.7001	-7.3666
12	CID_16486	101.105	3	2	-2.9545	-0.55335
13	CID_7983	144.213	2	0	2.3527	-7.6022
14	CID_66747	166.175	3	1	1.0522	-1.6196

Table 4: Docking scores and residues involved in H-bond formation

S/no	Compound ID	Docking score (kcal/mol)	Residues involve in H-bonds	Distance (Å)
1	CID_619544	-4.63	Thr169 Thr169	2.97 3.02
2	CID_619583	-5.91	0	0
3	CID_5732	-6.30	0	0
4	CID_616643	-5.62	Thr169	2.72
5	CID_240576	-4.33	0	0
6	CID_622021	-7.01	Thr169	3.06
7	CID_616496	-7.00	0	0
8	CID_590350	-7.08	0	0
9	CID_6586	-2.95	Arg183	2.97
10	CID_249920302	-	-	-
11	CID_13770	-3.49	Ser202	2.74
12	CID_16486	-4.64	Lys84 Tyr170 Asp40 Asp80	2.67 3.03 2.88 2.98
13	CID_7983	-4.23	Arg88 Leu206	2.85 2.90
14	CID_66747	-4.93	Glu205	2.99

Table 5: Pharmacokinetic analysis of constituents from the n-Butanol crude extract of *G.kola*

S/N	Compound name	BBB	CYP2D6 inhibitor	Mutagens	Tumorigens	Reproducibility	Irritant
1	CID_619544	no	no	high	None	none	none
2	CID_619583	yes	yes	none	None	none	high
3	CID_5732	Yes	yes	none	None	high	none
4	CID_616643	No	no	none	None	none	none
5	CID_240576	Yes	no	none	None	none	none
6	CID_622021	yes	No	high	None	none	none
7	CID_616496	No	no	low	None	none	none
8	CID_590350	No	no	low	None	none	none
9	CID_6586	Yes	no	high	High	none	low
10	CID_2499203 02	-	-	-	-	-	-
11	CID_13770	No	yes	none	None	none	none
12	CID_16486	No	no	none	None	none	None
13	CID_7983	Yes	no	high	None	none	None
14	CID_66747	Yes	no	none	None	high	High

Table 6: Predicative binding space, Surface area and Drug score

Compound	Binding space A ³	Surface area A ²	Drug score
CID_619544	242.18	250.61	0.45
CID_619583	-	-	-
CID_5732	242.18	350.61	0.45
CID_616643	243.18	350.61	0.45
CID_662021	242.18	350.61	0.45
CID_616496	176.58	389.51	0.34
CID_590350	242.18	359.61	0.45
CID_16486	916.61	894.72	0.82
CID_66747	250.30	413.0	0.72

Discussion

G. kola had been evaluated for its antibacterial properties including its activity against *Staph. aureus*; Ajayi *et al.*, (2014) evaluated the antibacterial activity of the seed extracts of *G. kola* against clinical dental isolates of *Staph* species; the ethanol extract showed an inhibitory activity of 13 and 14 at 400 mg/mL. Similar activity was reported on the seed, bark and root extract on *Staph. aureus* (Akelere *et al.*, 2008; Indabawa and Arzai, 2011; Ukaoma *et al.*, 2013).

The findings from this study highlighted the inhibitory antimicrobial activity of the root extract of *G. kola* on MDR *Staph. aureus*; significant activity was recorded by the chloroform, *n*-butanol and MeOH extracts (at the highest concentration) while no activity by *n*-hexane fraction. The *n*-butanol extract showed the highest mean zone of inhibition (18.50±0.41) at 100 mg/mL, followed by the chloroform (10.00±2.12) and MeOH (8.166±0.62) extracts, respectively;

however, the activity observed was lower compared to the standard drug, vancomycin (25.00±1.30) (Table1). This demonstrate that the bioactive constituents from the root of *G. kola* with antimicrobial effects are from the semi-polar/polar intermediate solvents. This collaborates the findings of Idu and colleagues on the chloroform root extract of *G. kola* against staph aureus (Idu *et al.*, 1970).

The *n*-butanol extract being the most active extract was subjected to further analysis using GC- MS in order to characterize the bioactive compounds and thus 14 different phytoconstituents with varying structural and physicochemical properties were obtained (Table 2). Some of the compounds exhibit benzoquinone, imidazole[1,2-*a*]pyridine, chlorocarbazole and azetidine scaffolds & motifs. Presence of this moieties in a compound attributes to its biological activity including potent antibacterial activity (Al-Tel *et al.*, 2011 and

da Silva *et al.*, 2020). Hence, the antibacterial activity exhibited by the *n*-butanol extract might be attributed to the presence of these compounds.

To investigate this claim, an *insilico* studies was performed using these compounds; the physiochemical analysis of drug likeness and Lipinski's rule of five (LO5) (Table 3) and molecular docking analysis against *Staph. aureus* tyrosyl-tRNA synthetase was evaluated; a bacterial drug target that is implicated in protein synthesis (Table 4). The results indicated that, the compounds had good physiochemical and drug likeness score. In the molecular docking analysis, 2-Hydroxy-3-(thiophen-2-yl)methyl-5-methoxy-1,4-benzoquinone, 9,9-Dichloro-9-silafluorene, Zolpidem, Pyridazine-3,5-dicarbonitrile, 1,6-dihydro-4-amino-6-imino-1-(2- nitrophenyl)-, 5H-Naphtho[1,8-bc]thiophen-5-one, 3,4-dihydro-2-phenyl-, 9,9'-Bis(3,6- dichlorocarbazole, 3,8-Di-*t*-butyl-5,6-diphenyl-2,9-dithia-1-phosphabicyclo[4.3.0]nona-3,7-diene 1-sulfide, (S)-(-)-2-Azetidinecarboxylic acid, and 2-Hydroxyethyl benzoate exhibited a good binding score ranging from -4.63 to -7.08 kcal/mol against the target protein and variable H-bondinteraction.

DoGSiteScorer was used to predict the binding pocket of the ligand. It employs the grid-based method that utilize the Difference of Gaussian filter to detect potential binding pockets solely based on the 3D structure of the protein; values are between zero and one and the higher the score the more drugable the pocket is estimated to be (Volkamer *et al.*, 2012). The selected compounds showed good drug score ranging from 0.45-0.82 (Table 6). Model interaction of the Protein-ligand is also analyzed and 2D structure

generated with PoseViewer (Fig 1-6). TyrRS is characterized by a α -helical domain, linked to the catalytic domain, and a C-terminal domain. The catalytic domain contains a six-stranded parallel β -sheet and a deep active-site cleft (Qui *et al.*, 2021). The authors also described the potential binding sides of inhibitors of TyrS; tyrosine, tyrosyl-AMP, ribose and tyrosinyl-adenylate complex.

Regarding their chemistry; **CID_619544** contains a 1,4-benzoquinone moiety, which is an essential structural unit of quinone compounds. Many natural derivatives has been isolated and synthesized, with potent antimicrobial activities documented (Abraham *et al.*, 2011). **CID_5732** is a imidazo[1,2-a]pyridine presents as an important scaffold in medicinal chemistry for development of active molecules. Many drugs had been designed to contain this active moiety including the antibiotic Rifaximin (Devi *et al.*, 2016) while **CID_616643** is a pyridazine dicarbonitrile derivative. **CID_16486** is an aliphatic heteromonocyclic compound. It's a natural azetidine derivative produced by plant as a protective agent against predators like insects. These compounds are non-proteinogenic amino acid homologue of proline, making them proline antagonist. These features make them potent antibiotics. Since then, several natural product and synthetic compounds having this amino acid moiety had been isolated and synthesize, offering a variety of pharmaceutical compounds including the antibiotic polyoxin(s) (Couty and Evano, 2006). Due to ring strain associated with it, azetidines are also useful synthons in organic chemistry (Brahmachari, 2015).

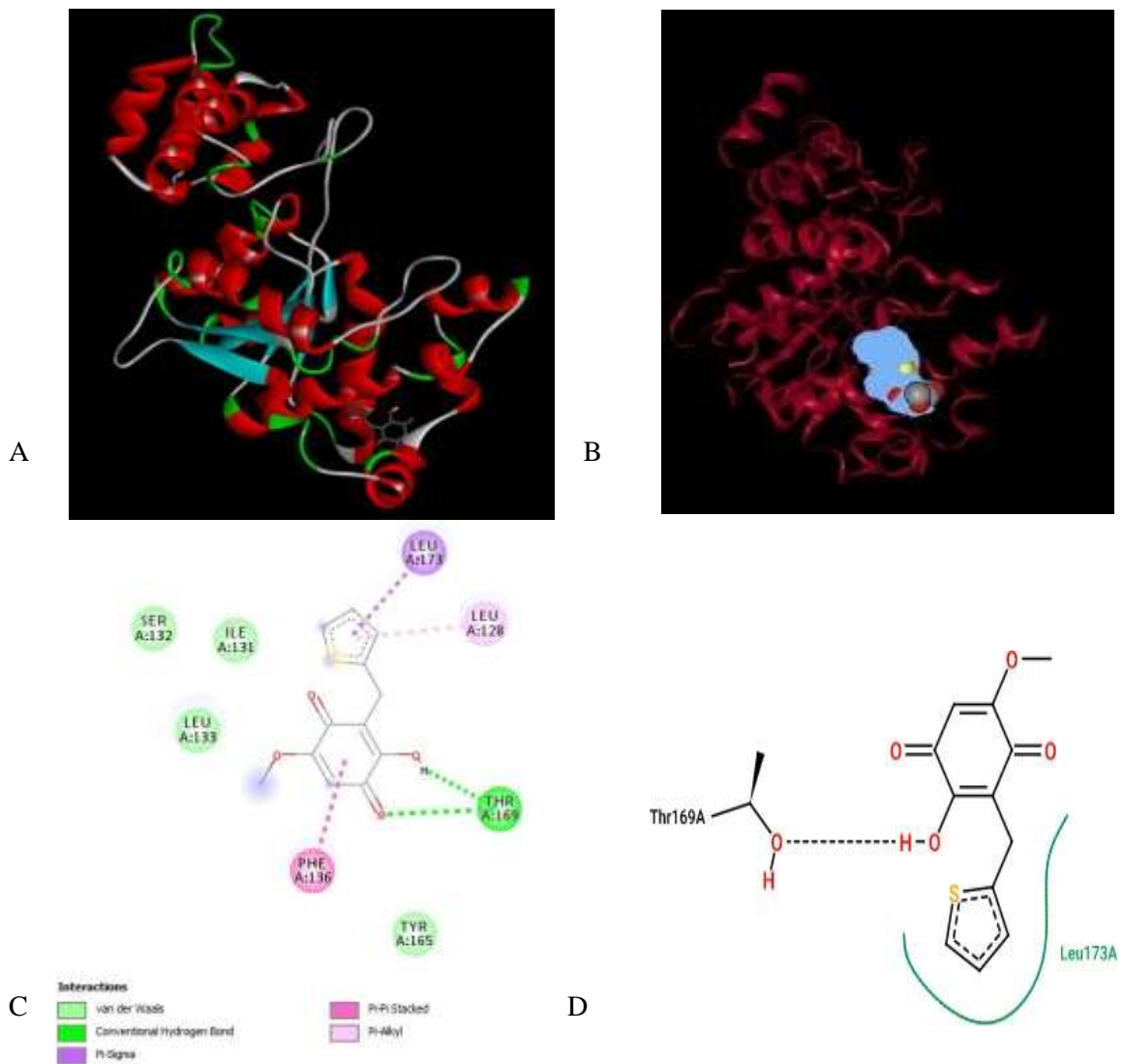


Fig 1: 2-Hydroxy-3-(thiophen-2-yl)methyl-5-methoxy-1,4-benzoquinone. **A**-protein-ligand complex. **B**-Ligand Binding Domain (LBD). **C and D**- 2D interaction model of CID_619544 and 1JJJ.

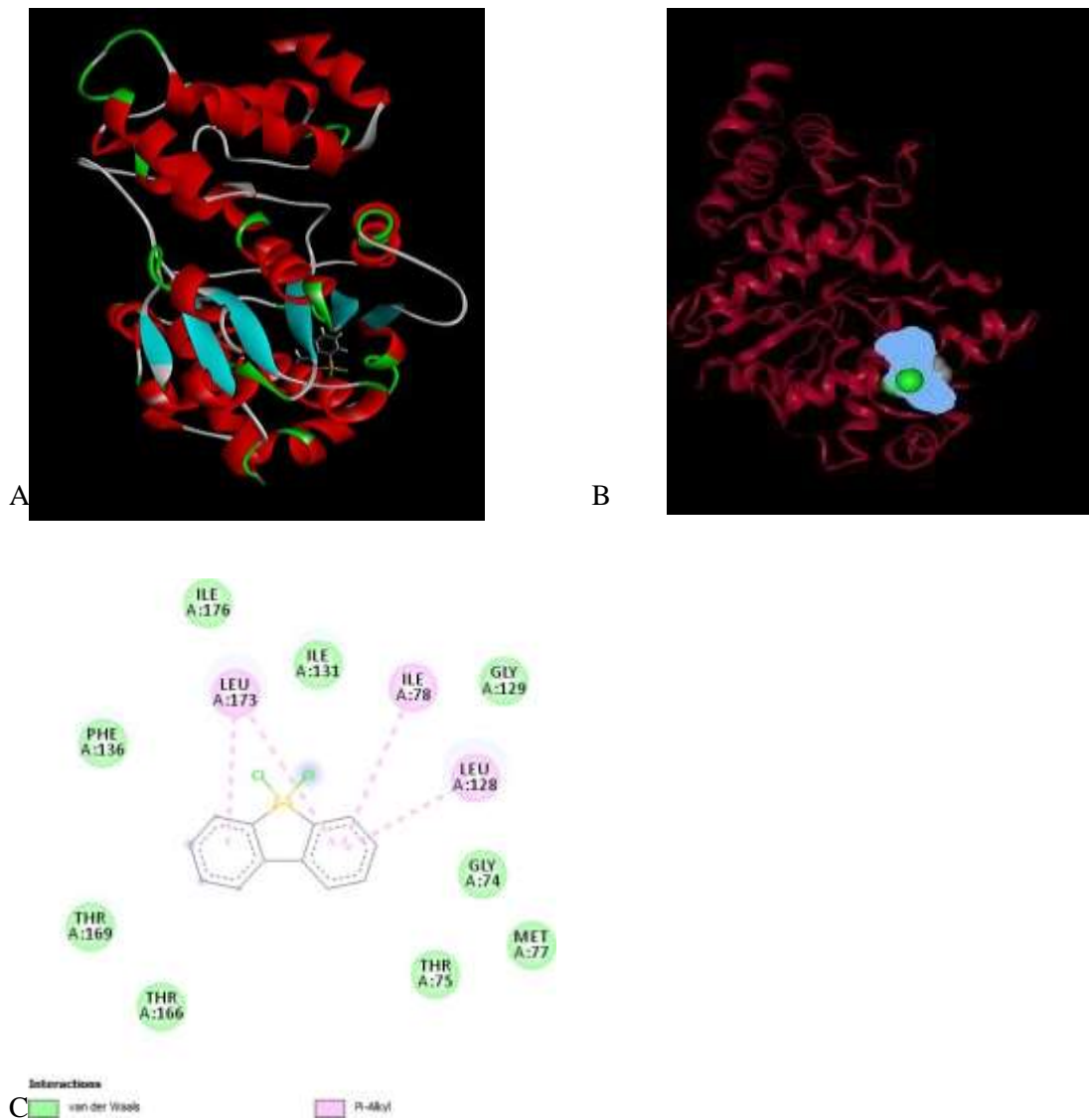


Fig 2: 9,9-Dichloro-9-silafluorene A-protein-ligand complex. B-Ligand Binding Domain (LBD). C - 2D interaction model of CID_619583 and 1JJJ.

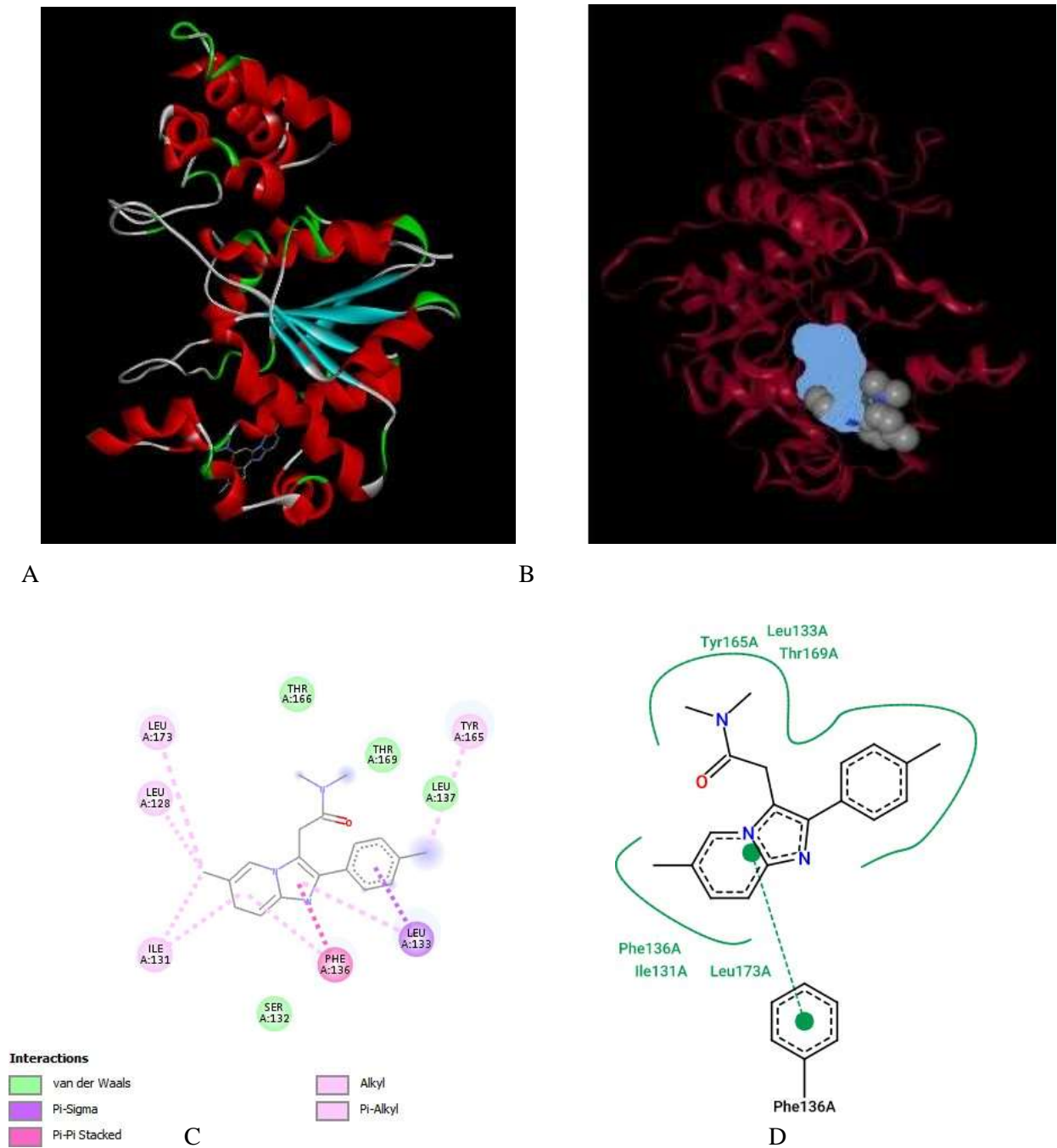


Fig 3: Zolpidem. A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_5732 and 1JJJ.

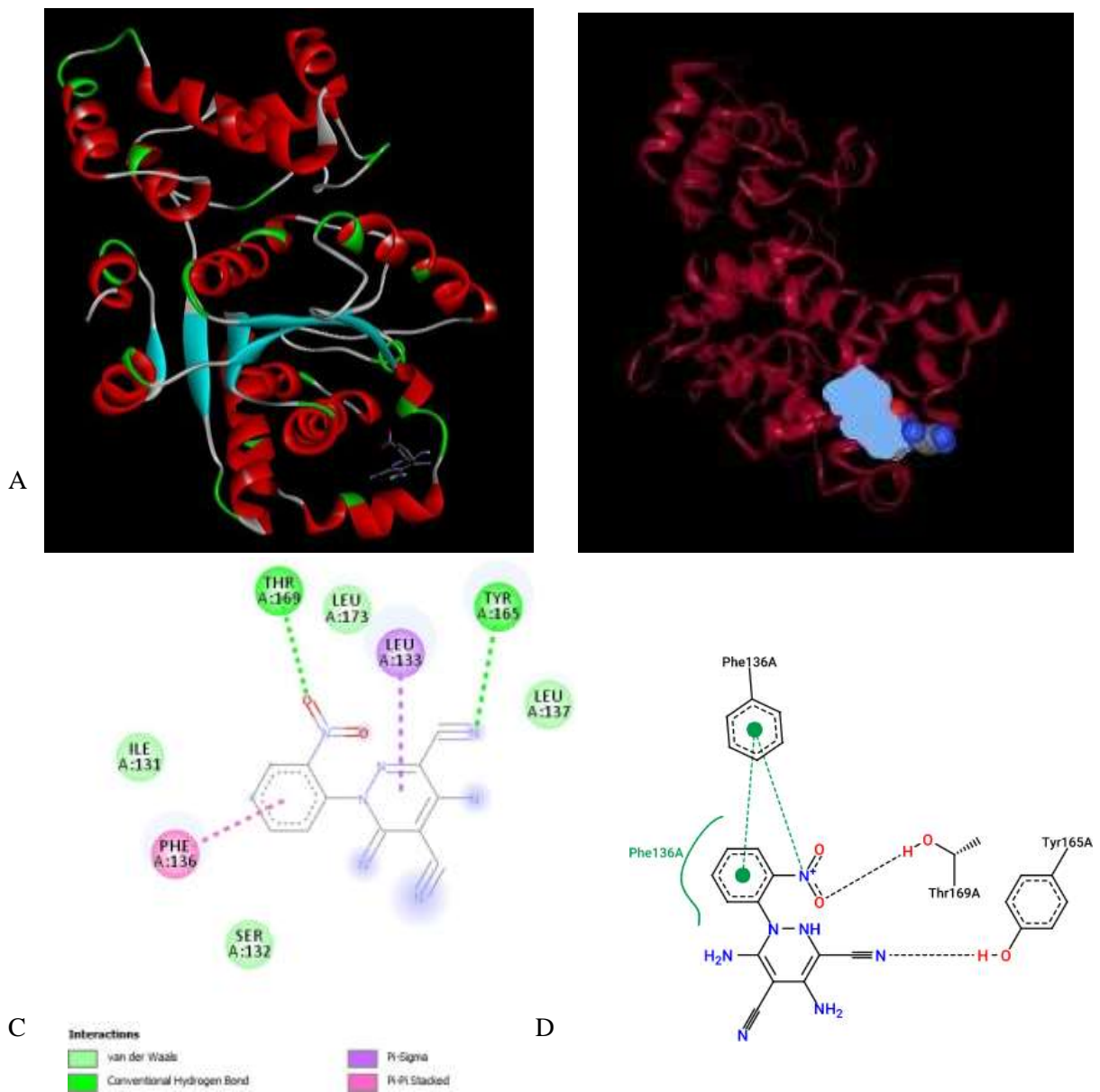


Fig 4: Pyridazine-3,5-dicarbonitrile, 1,6-dihydro-4-amino-6-imino-1-(2-nitrophenyl)-. **A**-protein-ligand complex. **B**-Ligand Binding Domain (LBD). **C** and **D**- 2D interaction model of CID_616643 and 1JJJ.

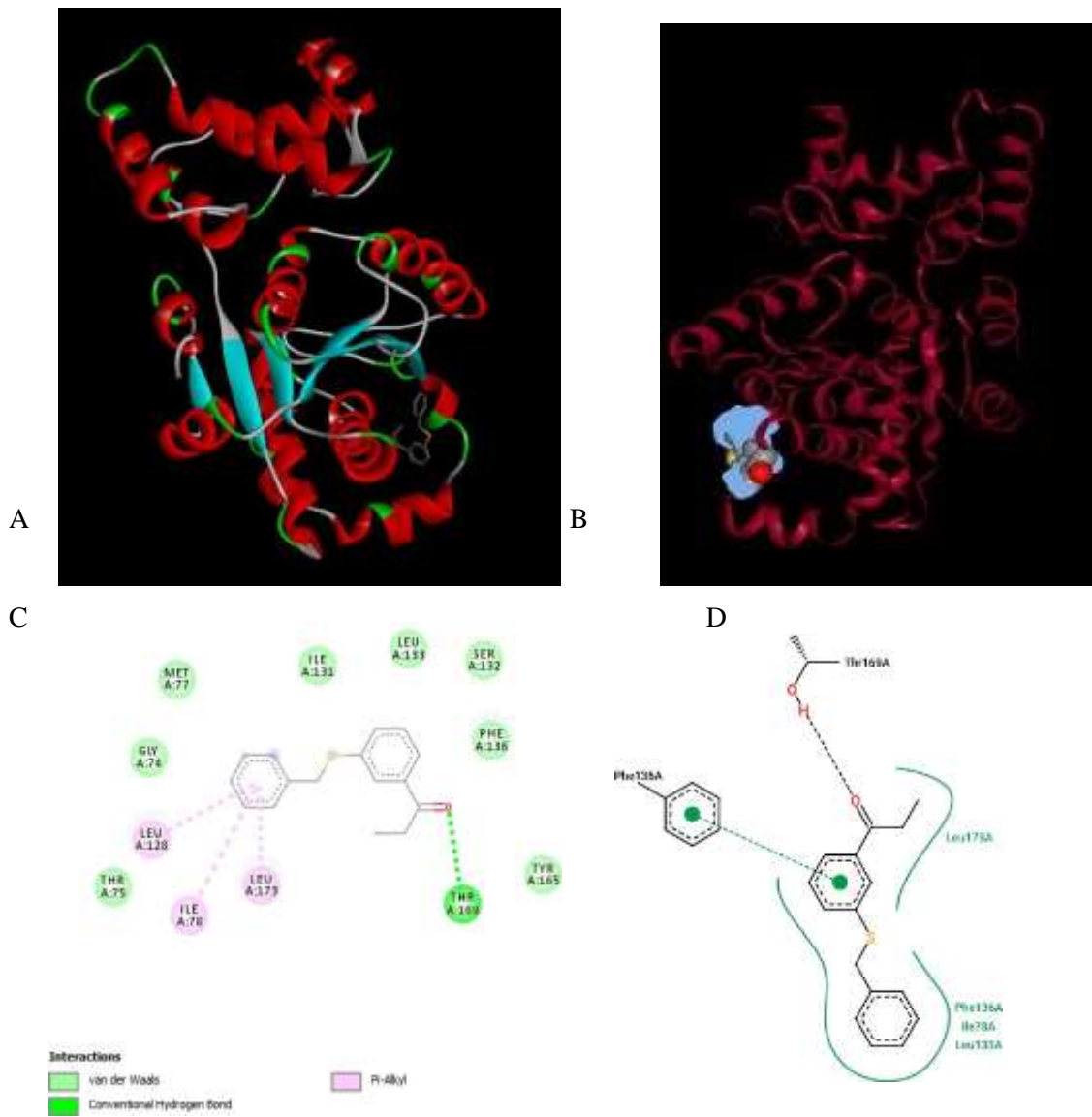


Fig 5: 5H-Naphtho [1,8-bc]thiophen-5-one, 3,4-dihydro-2-phenyl-. A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_622021 and 1JJJ.

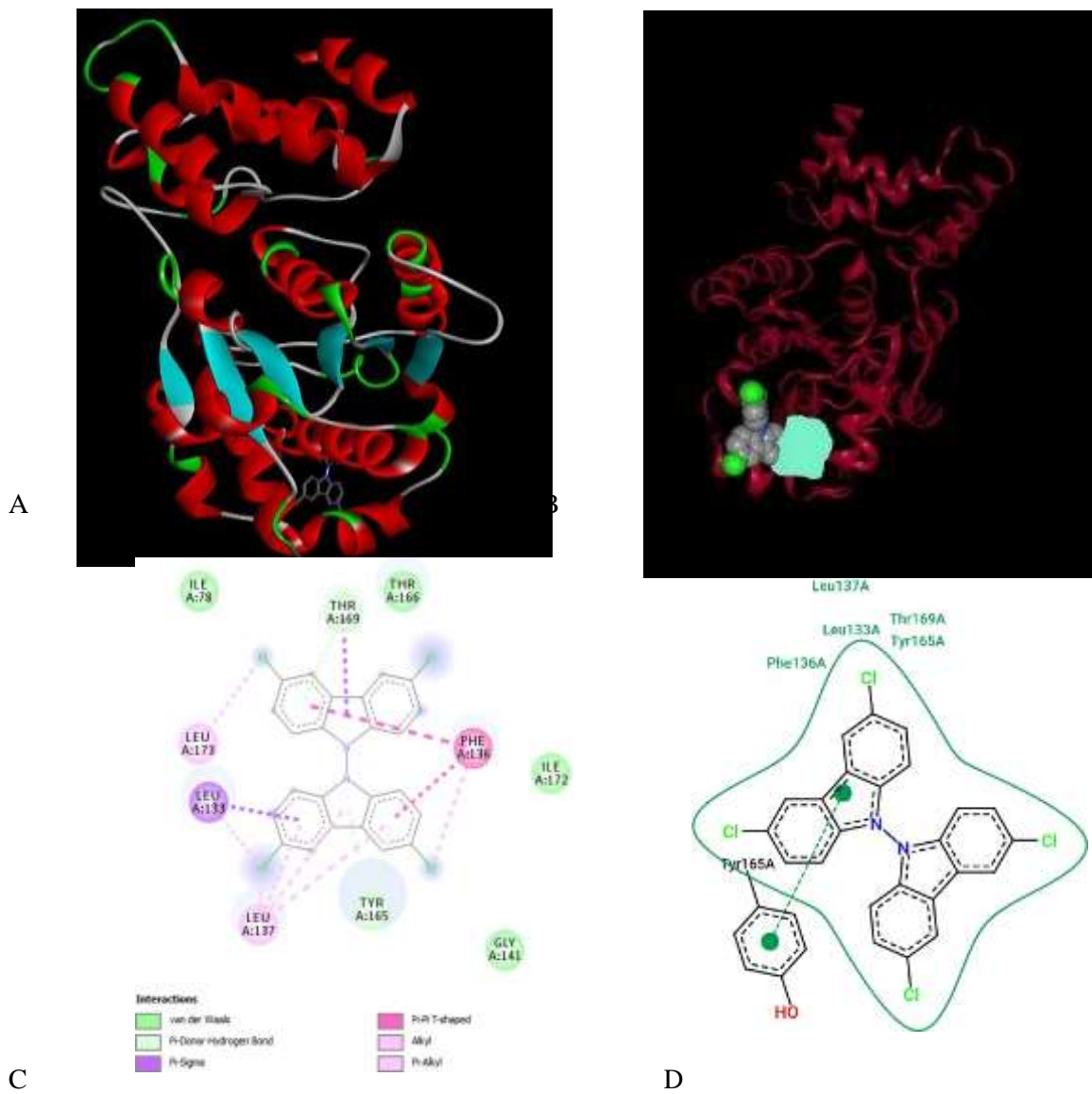


Fig 6: 9,9'-Bis(3,6-dichlorocarbazole) A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_616496 and 1JJJ.

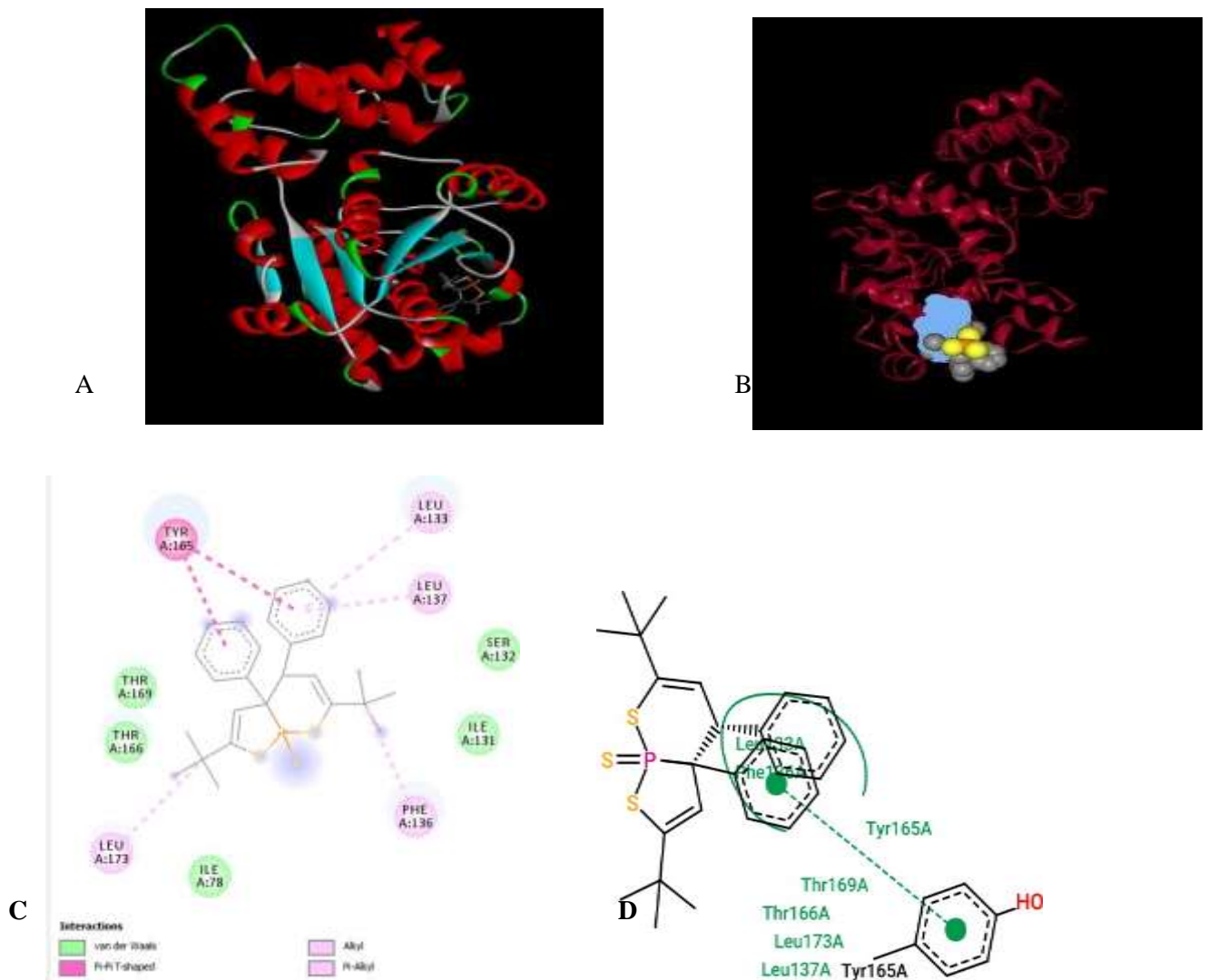


Fig 7: 3,8-Di-t-butyl-5,6-diphenyl-2,9-dithia-1-phosphabicyclo[4.3.0]nona-3,7-diene 1-sulfide. A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_590350 and 1JJJ.

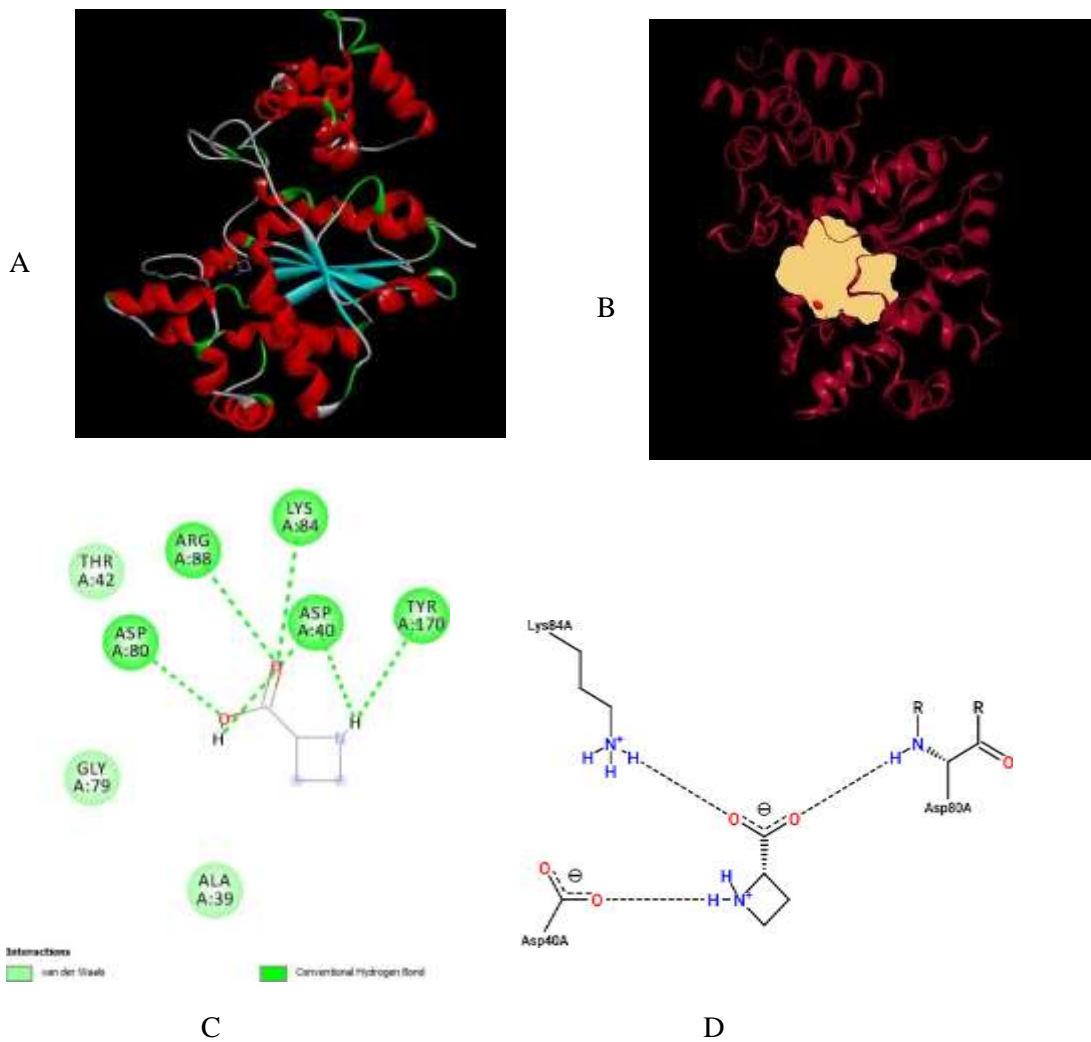


Fig 8: (S)-azetidine-2-carboxylic acid. A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_16486 and 1JIJ.

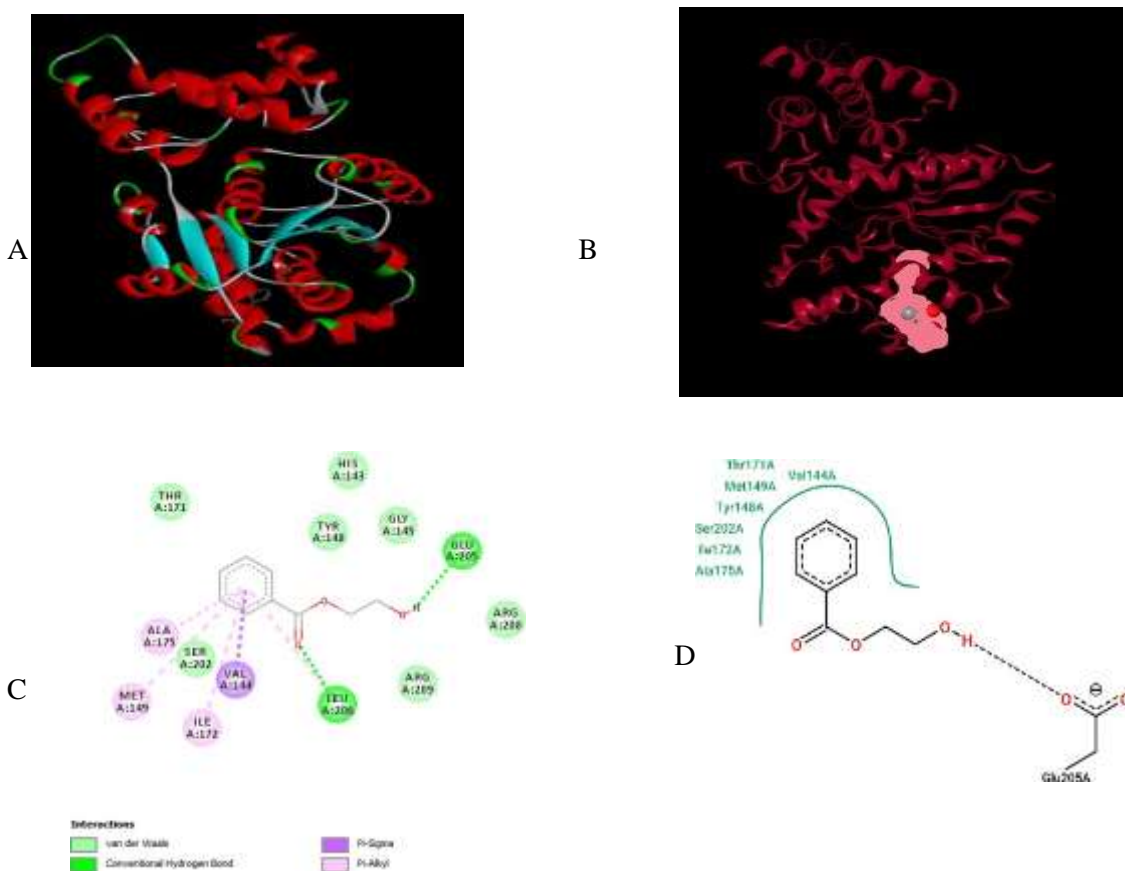


Fig 9: 2-hydroxyethyl benzoate. A-protein-ligand complex. B-Ligand Binding Domain (LBD). C and D- 2D interaction model of CID_66747 and 1JJ.

The root extracts of *Garcinia kola* showed promising activity against MDR *Staphylococcus aureus*. The n-Butanol fraction recorded the highest activity; and its phytoconstituents were explored using GC-MS analysis. A Total of 14 compounds were obtained and subjected to physicochemical analysis and insilico molecular docking studies; which determine their binding energies against *Staphylococcus aureus* tyrosyl-tRNA synthetase and the result of the docking studies showed that 9 compounds including CID_619544, CID_619583, CID_5732, CID_616643, CID_622021,

CID_616496, CID_590350, CID_16486 and CID_66747 exhibited good docking with CID_590350 having the highest score. Further analysis for Pharmacokinetic parameters was recorded. Thus, these compounds from *G. kola* are proposed to be potential inhibitors of tyrosyl-tRNA synthetase and effective against MDR *Staphylococcus aureus* after successful experimental validation.

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Conflict of interest

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