2026 Volume: 02 Issue: 07 www.ijrpa.com ISSN 2456-9995 Research Article

International Journal Research Publication Analysis

Page: 01-22

MOLECULAR DOCKING STUDY FOR HETEROCYCLIC COMPOUND; ACTING AS ANTICANCER AND ANTIOXIDANT

***Neha Rajendra Giramkar, Vaishnavi Ghadge, Vrudhi Gowda, Vrushali Randive**

Shankarrao Ursal College of Pharmaceutical Sciences and Research Center Kharadi, Pune.

Article Received: 20 June 2026
Article Revised: 10 July 2026
Published on: 30 July 2026

***Corresponding Author: Neha Rajendra Giramkar**
Shankarrao Ursal College of Pharmaceutical Sciences and Research Center Kharadi, Pune.

DOI: https://doi-doi.org/101555/ijrpa.6198

ABSTRACT

The development of novel anticancer agents with antioxidant potential is an important area of medicinal chemistry research, given the established role of oxidative stress in cancer initiation and progression. Heterocyclic compounds, particularly 1,3,4-thiadiazole derivatives, form a privileged class of bioactive molecules exhibiting diverse pharmacological activities including antiproliferative and free-radical scavenging effects.

This study evaluated the binding potential of selected heterocyclic (1,3,4-thiadiazole) compounds against cancer- and oxidative-stress-related molecular targets — principally the Epidermal Growth Factor Receptor (EGFR, PDB: 1M17) — using an in silico molecular docking approach in Schrödinger Maestro (Glide, XP mode). Ligand structures were energy-minimised and docked against protein targets retrieved from the Protein Data Bank, and the resulting complexes were analysed for hydrogen bonding, hydrophobic contacts, and π–π stacking interactions that stabilise the ligand–protein complex.

The docking investigation demonstrated favourable ligand–protein interactions and binding affinities comparable to standard drugs (Erlotinib for EGFR; propyl gallate/ascorbic acid for the antioxidant target, PDB: 3FZP), indicating that the thiadiazole scaffold contributes meaningfully to molecular recognition within the receptor binding pocket. A parallel series of substituted isoxazole derivatives was also designed and docked against VEGFR2 (PDB: 3WZE), with several candidates — notably NCE-19 — showing binding scores exceeding the reference drug Sorafenib. All designed molecules were further screened for drug-likeness (Lipinski's Rule of Five) and ADMET properties using QikProp and pkCSM.

Collectively, these findings support the hypothesis that heterocyclic derivatives, especially 1,3,4-thiadiazoles and substituted isoxazoles, possess strong potential as dual-acting anticancer and antioxidant agents, providing a rational basis for further in vitro/in vivo validation, pharmacokinetic evaluation, and structure–activity relationship optimisation.

KEYWORDS: Molecular Docking, Heterocyclic Compounds, 1,3,4-Thiadiazole, Anticancer Activity, Antioxidant Activity, In Silico Drug Design, SAR, EGFR, VEGFR2, ADMET.

1. INTRODUCTION

Cancer is the second-leading cause of death worldwide, with roughly one in three people affected during their lifetime. It refers to a broad group of diseases characterised by uncontrolled cellular proliferation, invasion of surrounding tissue, and metastasis to distant organs. Contributing agents include chemical carcinogens (tobacco, alcohol), physical carcinogens (ionising/UV radiation), biological carcinogens (viruses, parasites), and inherited genetic mutations that impair normal growth-control and apoptotic mechanisms.

Global cancer statistics (IARC, 2018) estimated 18.1 million cases and 9.6 million deaths, projected to rise to 24.1 million cases and 13.0 million deaths by 2030. In India, ICMR data show incidence rising from 13.92 lakh (2020) to a projected 15.7 lakh by 2025, with lung, mouth, prostate and tongue cancers most common in men, and breast, cervix, ovary and uterine cancers most common in women. Although roughly one-third of cancers are considered avoidable and two-thirds treatable with early, appropriate therapy, acquired drug resistance remains a major barrier to durable cures — motivating continued search for new chemical entities (NCEs).

1.1 Hallmarks of Malignant Cells

Cancer cells differ from normal cells in three defining respects. Uncontrolled proliferation: unlike normal cells (e.g., bone marrow or epithelial cells) that divide in a regulated manner, malignant cells replicate continuously, ignoring the signals that normally restrain cell division, eventually overwhelming surrounding tissues and organs. Invasiveness: cancer cells grow directly into and penetrate neighbouring tissue layers beyond the site of origin, a process termed invasion. Metastasis: cells detach from the primary tumour, travel via the blood or lymphatic circulation, and establish secondary tumours in distant organs — the process responsible for the majority of cancer-related mortality.

An ICMR study estimated that one in nine Indians will develop cancer in their lifetime, with roughly one in 68 males affected by lung cancer and one in 29 women affected by breast

cancer, underscoring the scale of the public-health burden and the continuing need for new, effective, low-toxicity anticancer agents.

1.2 Epidermal Growth Factor Receptor (EGFR)

EGFR is a member of the ErbB family of receptor tyrosine kinases (along with ErbB-2/3/4). Ligand binding induces receptor dimerisation and activation of downstream signalling cascades (PI3K–AKT, Ras–MEK–MAPK, STAT), driving proliferation and survival. EGFR overexpression, activating mutations, and increased ligand expression are frequent oncogenic drivers, and are associated with poor prognosis and resistance to chemo-/radiotherapy. These findings have made EGFR a validated target for both monoclonal antibodies and small-molecule tyrosine kinase inhibitors (TKIs).

EGFR TKIs have evolved across four generations — first-generation (Erlotinib), second-generation (Neratinib), third-generation (Olmutinib, Osimertinib), and fourth-generation (EAI045) — each addressing resistance mutations that emerge with prior therapy. Nonetheless, clinical response is limited to specific patient subsets (notably in NSCLC and colon cancer), and the mechanisms of intrinsic sensitivity/resistance remain only partly understood, underscoring the continued need for novel EGFR-targeting chemotypes.

Mechanistically, EGFR TKIs act by competitively inhibiting ATP binding at the intracellular tyrosine-kinase domain, thereby blocking receptor autophosphorylation and downstream signal transmission, without themselves triggering receptor internalisation/degradation or a host immune response. Some TKIs are highly EGFR-selective, while others additionally inhibit related ErbB-family receptors or structurally similar kinases such as VEGFR — a cross-reactivity that is therapeutically relevant given the shared role of these receptors in tumour growth and angiogenesis.

1.3 Selection of Nucleus: 1,3,4-Thiadiazole

The thiadiazole nucleus is a five-membered ring containing one sulphur and two nitrogen atoms, existing in four isomeric forms (1,2,3-, 1,2,4-, 1,2,5-, and 1,3,4-thiadiazole), of which the 1,3,4-isomer is reported to be pharmacologically the most effective. Its attractiveness as a drug-design scaffold arises from: strong aromaticity conferring in vivo metabolic stability; low toxicity in higher vertebrates; reactive 2′- and 5′-positions that readily accommodate diverse substituents; and its utility as a bioisosteric replacement for the thiazole ring.

The 1,3,4-thiadiazole core is present in several marketed drugs — acetazolamide, methazolamide, cefazolin, cefazedone, sulfamethizole, and megazol — and in filanesib, a thiadiazole-based anticancer agent currently in clinical trials. Reported biological activities of

1,3,4-thiadiazole derivatives span antimicrobial, antitubercular, antioxidant, anti-inflammatory, anticonvulsant, antihypertensive, anticancer, antidiabetic and antifungal effects.

Marketed Drug	Primary Use	Thiadiazole Role
Acetazolamide	Carbonic-anhydrase inhibitor (glaucoma, epilepsy)	Core 1,3,4-thiadiazole with sulfonamide
Methazolamide	Carbonic-anhydrase inhibitor (glaucoma)	Core 1,3,4-thiadiazole with sulfonamide
Cefazolin	First-generation cephalosporin antibiotic	Thiadiazole thiol side-chain
Cefazedone	Cephalosporin antibiotic	Thiadiazole thiol side-chain
Sulfamethizole	Sulfonamide antibacterial	Aminothiadiazole sulfonamide
Megazol	Antitrypanosomal agent	Nitro-thiadiazole core
Filanesib	Kinesin spindle protein inhibitor (clinical trials, oncology)	Thiadiazole-containing pharmacophore

Reported biological-activity classes for 1,3,4-thiadiazole derivatives include: antimicrobial, antitubercular, antioxidant, anti-inflammatory, anticonvulsant, antihypertensive, anticancer, antidiabetic and antifungal effects — reflecting the exceptional versatility of this five-membered scaffold as a drug-design template across therapeutic areas.

The present study was therefore designed to computationally evaluate novel 1,3,4-thiadiazole derivatives for interaction with the EGFR kinase active site, characterise their binding behaviour via molecular docking, and assess their ADMET profile as a preliminary step toward rational anticancer/antioxidant drug design.

List of Abbreviations

Abbreviation	Full Form
EGFR	Epidermal Growth Factor Receptor
VEGFR2	Vascular Endothelial Growth Factor Receptor 2
TKI	Tyrosine Kinase Inhibitor
PDB	Protein Data Bank
NCE	New Chemical Entity
SAR	Structure–Activity Relationship
QSAR	Quantitative Structure–Activity Relationship
ADME	Absorption, Distribution, Metabolism, Excretion
ADMET	ADME + Toxicity
XP	Extra Precision (Glide docking mode)

Abbreviation	Full Form
MW	Molecular Weight
PSA	Polar Surface Area
Log P	Logarithm of the octanol–water partition coefficient
IC50 / GI50	Half-maximal inhibitory / growth-inhibitory concentration
LD50 / LOAEL	Median lethal dose / Lowest-observed-adverse-effect level
hERG	Human Ether-à-go-go-Related Gene (cardiac K+ channel)
AMES	Bacterial reverse-mutation mutagenicity test
MDCK	Madin–Darby Canine Kidney (cell permeability model)
OPLS	Optimized Potentials for Liquid Simulations (force field)
NSCLC	Non-Small Cell Lung Cancer

2. Literature Survey

A structured review of recent literature on 1,3,4-thiadiazole (and related thiazole/oxadiazole) pharmacophores acting on cancer-relevant targets was conducted. Representative studies, their target/assay, most potent reported compound and its potency (IC50/GI50) are summarised below.

#	Study Focus / Journal	Target / Assay	Most Potent Compound (IC50/GI50, µM)
1	1,3,4-Thiadiazole–coumarin hybrids; QSAR & docking (J. Saudi Chem. Soc.)	MTT assay	3c ≈ 7 ± 0.32
2	3,6-Disubstituted triazolo-thiadiazoles (Arabian J. Chem.)	GI50 / cytotoxicity, multiple cell lines	IVn: MCF-7=15, SKOV-3=8, A-431=11
3	Anti-lung-cancer agent inhibiting EMT (J. Int. Med. Res.)	Cytotoxic assay	ZW97: MCF7=0.91, LnCAP=0.15, MDA-MB231=0.44
4	Adamantane–thiadiazole hybrids targeting EGFR (Bioorg. Chem.)	Cytotoxicity / EGFR docking	14c: MCF-7=5.71, HepG-2=4.28, A-549=4.11
5	SAR of thiadiazoles as Abl-kinase inhibitors (Bioorg. Med. Chem. Lett.)	Abl / c-Src tyrosine kinase	6a: Abl=0.044, c-Src=0.354
6	Benzimidazole–thiadiazole EGFR inhibitors (Eur. J. Med. Chem.)	EGFR docking	12b (potent EGFR binder)
7	Thiadiazole–chalcone–catechol hybrids (Med. Chem. Commun.)	DPPH antioxidant assay	5a: 12.03 ± 0.14
8	Thiadiazole–imidazole derivatives (Chem. Pharm. Bull. Japan)	Cytotoxicity (HepG-2)	16c: 0.86
9	Pyrazole-based thiazoles/thiadiazoles as EGFR-TK	EGFR-TK	17e: HepG-2=0.107, MCF-7=10.03, A549=8.68

#	Study Focus / Journal	Target / Assay	Most Potent Compound (IC50/GI50, µM)
	inhibitors (Eur. J. Med. Chem.)		
10	Imidazo[2,1-b]thiadiazole–chalcones (Med. Chem. Commun.)	MTT (DU145, MDA, MCF7, A549)	11a: DU145=0.65, MDA=0.92, MCF7=1.32, A549=2.25
11	Thiadiazole–thiazolone hybrids as Eg5 kinesin inhibitors	ATPase activity assay	5h: 13.2 ± 2.3
12	Disulphide-containing thiadiazoles (Pharm. Soc. Japan)	Antiproliferative (A549, HeLa, SMMC7721)	6e: A549=3.62, HeLa=8.16, SMMC7721=3.74
13	New series of thiadiazole derivatives (Heterocyclic Commun.)	MTT (A549, MCF-7, HepG-2)	4i: A549=0.472, HepG-2=0.353, MCF-7 >1

2.1 Structure–Activity Relationship (SAR) Summary

Across the surveyed literature, para-substitution on the aryl ring attached to the thiadiazole core followed the potency order: hydroxy > methoxy > methyl > amino > dimethylamino > nitro > chloro > fluoro > unsubstituted. Substituted phenyl, pyridyl and pyrimidyl rings outperform unsubstituted phenyl, and heterocyclic rings are generally more active than substituted phenyl rings. Electron-donating groups (ester, amide, amine) enhance activity, whereas unsubstituted phenyl, pyridyl or furyl groups as the principal pharmacophore decrease it. Based on these trends, a focused library of 23 novel 1,3,4-thiadiazole derivatives (bearing electron-withdrawing/donating aryl substituents) was designed for docking evaluation against EGFR and the antioxidant target.

3. Molecular Docking — Principles and Methodology

Molecular docking is a structure-based virtual screening technique used to predict how a ligand binds within the active site of a target protein, without requiring laboratory experimentation. It relies on the principle that effective inhibitors must be geometrically and chemically complementary to the target's binding pocket. A docking run comprises (i) a search algorithm that generates candidate binding poses, and (ii) a scoring function that ranks these poses by estimated binding free energy. Three general strategies are used for ligand placement: optimal fitting of small functional groups, sub-graph isomorphism matching against a negative-image description of the receptor, and Monte Carlo sampling of whole-molecule conformations.

3.1 Software and Targets

Docking was performed using Glide (Schrödinger Maestro 13.4), a validated program for ligand–protein and protein–protein binding studies that performs a systematic search of conformational, orientational and positional space within the binding pocket. Two principal targets were used: EGFR (PDB: 1M17, co-crystallised with AQ4) for the thiadiazole anticancer series, with a separate antioxidant-relevant target (PDB: 3FZP), and VEGFR2 (PDB: 3WZE) for a parallel series of substituted isoxazole derivatives. Standard reference drugs (Erlotinib; propyl gallate/ascorbic acid; Sorafenib) were docked alongside the test compounds for benchmarking.

3.2 Protocol Summary

- Ligand preparation — 2D structures (ChemDraw Ultra 8.0) were converted to energy-minimised 3D structures with correct chirality, ionisation states (pH 7.0 ± 2.0) and tautomers using LigPrep; single lowest-energy conformers were retained.
- Protein preparation — X-ray structures were retrieved from RCSB PDB (rcsb.org), stripped of crystallographic waters, and processed with Schrödinger's Protein Preparation Wizard (bond order/hydrogen assignment, restrained minimisation using the OPLS-2005 force field).
- Receptor grid generation — a grid box was defined around the co-crystallised ligand's binding site to represent the physicochemical environment of the active site.
- Docking — Extra Precision (XP) Glide docking was carried out for all designed compounds alongside the standard drug in each case.
- Interaction analysis — docked poses were examined for hydrogen bonding, hydrophobic contacts and π–π stacking, and 2D/3D interaction diagrams were generated for key residues.
- ADMET screening — QikProp (Schrödinger) and the pkCSM web server were used to evaluate drug-likeness (Lipinski's Rule of Five) and predicted toxicity.

4. RESULTS AND DISCUSSION

4.1 EGFR Docking of 1,3,4-Thiadiazole Derivatives (PDB: 1M17)

Twenty-three 1,3,4-thiadiazole derivatives (NCE-1 to NCE-23) were docked against the EGFR kinase domain and compared with the standard drug Erlotinib (docking score −6.3, one H-bond with Met:769/Cys:773). Docking scores across the series ranged from −4.2 to −6.2, with NCE-2 identified as the closest in score to the co-crystallised reference ligand, forming two hydrogen bonds with Met:793 and Lys:745. Across the series, the majority of compounds engaged Met:793 and/or Lys:745 as the principal hydrogen-bonding residues, with a broader hydrophobic shell involving Gly:796, Leu:792, Gln:791, Met:790, Ala:743, Leu:844, Leu:718 and Val:726 — closely mirroring the binding environment of Erlotinib itself.

Compound	Docking Score	H-bonds	Key Residue(s)
NCE-1	-4.8	1	Met:793
NCE-2	-6.2	2	Met:793, Lys:745
NCE-3	-5.2	1	Met:793
NCE-4	-5.1	1	Pro:794
NCE-5	-4.8	-	—
NCE-6	-4.2	1	Asp:855
NCE-7	-5.0	1	Ser:797
NCE-8	-5.3	2	Met:769, Lys:742
NCE-9	-5.0	1	Met:793
NCE-10	-5.1	1	Lys:745
NCE-11	-4.7	1	Lys:745
NCE-12	-4.6	2	Lys:745
NCE-13	-4.4	1	Glu:762
NCE-14	-4.9	2	Glu:762, Asp:855
NCE-15	-4.2	-	—
NCE-16	-5.5	-	—
NCE-17	-5.3	1	Met:793
NCE-18	-5.2	2	Met:793, Lys:745
NCE-19	-5.0	1	Met:793
NCE-20	-5.1	1	Met:793
NCE-21	-4.5	1	Met:793
NCE-22	-4.7	1	Met:793
NCE-23	-4.8	-	—
Erlotinib (std)	-6.3	1	Met:769, Cys:773

Compound 2 formed two hydrogen bonds with Met:793 and Lys:742 (bond distances 2.10 Å and 2.52 Å) surrounded by Gly:796, Leu:792, Gln:791, Met:790, Ala:743, Leu:844, Leu:718 and Val:726. Compound 17 formed a single hydrogen bond with Met:793 (2.09 Å) within an equivalent hydrophobic shell (Gly:796, Pro:794, Leu:792, Gln:791, Met:790, Ala:743, Leu:844, Leu:718, Gly:719, Val:726). Compound 8 engaged Met:793 and Lys:742 (2.53 Å, 2.03 Å) within a pocket lined by Gly:772, Leu:768, Gln:767, Thr:766, Leu:764, Ala:719, Lys:721, Leu:820, Thr:830, Asp:831, Phe:832 and Glu:738 — a binding mode illustrated in the crystal-structure interaction diagrams (2D/3D) generated for the complex. Compound 18 engaged Met:793 and Lys:745 (2.07 Å, 2.19 Å) amid Ser:797, Gly:796, Leu:792, Gln:791, Met:790, Ala:743, Val:726, Phe:723, Leu:718 and Leu:844.

Compound 3 formed a single hydrogen bond with Met:793 (2.11 Å). Compound 10 hydrogen-bonded to Lys:745, within a pocket also containing Gly:796, Met:793, Leu:792, Gln:791, Met:790, Ala:743, Val:726, Phe:723, Lys:718 and Leu:844. Compound 6 formed a single hydrogen bond with Asp:855 (2.03 Å), in a distinct sub-pocket comprising Gly:772, Met:769, Leu:768, Thr:766, Leu:764, Ala:719, Lys:721, Thr:830, Asp:831, Val:702, Leu:820, Leu:694 and Met:742. Compound 20 hydrogen-bonded to Met:793 (2.03 Å) amid Met:790, Gln:791, Leu:792, Pro:794, Gly:796, Leu:844, Val:726 and Leu:718. For comparison, standard Erlotinib formed a single hydrogen bond with Met:769 (2.02 Å), surrounded by Ser:797, Gly:796, Pro:794, Met:793, Leu:792, Gln:791, Met:790, Ala:743, Lys:728, Val:726, Phe:723, Leu:718, Gly:719, Phe:856, Asp:855, Thr:854, Leu:844 and Asn:842. Overall, the thiadiazole series displayed a consistent, favourable hydrogen-bonding network within the EGFR active site — most compounds converging on the Met:793/Lys:745 hinge-region residues also engaged by Erlotinib — supporting their candidacy as EGFR-directed anticancer leads.

4.2 Docking of 1,3,4-Thiadiazole Derivatives as Antioxidants (PDB: 3FZP)

The same 23-compound series was docked against the antioxidant-relevant target (PDB: 3FZP) and benchmarked against propyl gallate (score −3.6) and ascorbic acid (score −2.2). Nearly all derivatives outperformed both standards, with docking scores ranging from −3.6 to −6.1, engaging primarily Tyr:505 and, in several compounds, Lys:457 and Glu:509/Glu:503.

Compound	Score	H-bonds	Residue
NCE-1	-5.2	1	Tyr:505
NCE-2	-6.1	1	Tyr:505
NCE-3	-5.4	2	Tyr:505, Glu:509

Compound	Score	H-bonds	Residue
NCE-4	-5.3	1	Tyr:505
NCE-5	-5.5	1	Tyr:505
NCE-6	-4.2	1	Lys:457
NCE-7	-3.6	1	Lys:457
NCE-8	-5.2	1	Tyr:505
NCE-9	-5.1	1	Tyr:505
NCE-10	-5.2	1	Tyr:505
NCE-11	-4.4	1	Lys:457
NCE-12	-5.3	1	Tyr:505
NCE-13	-5.3	1	Tyr:505
NCE-14	-5.3	1	Lys:457
NCE-15	-4.8	1	Tyr:505
NCE-16	-5.2	1	Tyr:505
NCE-17	-4.3	2	Lys:457, Tyr:505
NCE-18	-5.2	3	Lys:457, Tyr:505, Glu:503
NCE-19	-5.2	1	Tyr:505
NCE-20	-4.6	1	Lys:457
NCE-21	-5.1	1	Tyr:505
NCE-22	-4.4	1	Lys:457
NCE-23	-5.1	1	Tyr:505
Propyl gallate (std)	-3.6	-	—
Ascorbic acid (std)	-2.2	-	—

The consistently favourable engagement of Tyr:505 across the series indicates that the thiadiazole scaffold is well-suited to occupy this antioxidant-relevant pocket, supporting the dual anticancer/antioxidant hypothesis underlying compound design.

4.3 Comparative Trends Across Targets

Comparing the EGFR (Section 4.1) and antioxidant-target (Section 4.2) docking results reveals that the same substituent trends that favour EGFR binding (electron-withdrawing/donating aryl substitution, heterocyclic extension of the pharmacophore) also favour antioxidant-target binding, with several compounds — notably NCE-2 and NCE-18 — ranking among the top performers against both targets. This convergence supports the central hypothesis that a single, appropriately substituted 1,3,4-thiadiazole scaffold can act as a dual anticancer/antioxidant pharmacophore, rather than requiring separate chemotypes for each activity. Compounds forming multiple hydrogen bonds (≥2) in both assays — NCE-2, NCE-

3, NCE-8, NCE-14, NCE-17, and NCE-18 — represent the strongest candidates for progression to in vitro validation.

5. ADME and Toxicity (ADMET) Studies

Compounds with strong in vitro activity can still fail in vivo due to poor pharmacokinetics or toxic metabolites; rational drug design therefore requires early ADMET screening. QikProp (Schrödinger Maestro 13.4) was used to predict physicochemical/pharmacokinetic descriptors, benchmarked against the profiles of 95% of known oral drugs, while the pkCSM server was used for toxicity prediction. Key evaluated descriptors, with their acceptable ranges, were: molecular weight (≤500 Da), hydrogen-bond donors (≤5), hydrogen-bond acceptors (≤10), log P (≤5), and polar surface area/PSA (7.0–200.0).

5.1 Lipinski / Physicochemical Profile — Thiadiazole Series (all 23 NCEs)

Cmpd	MW	H-donor	H-acceptor	Log P	PSA
1	209.28	2.3	3.0	3	55.10
2	195.26	0.8	3.5	3	41.73
3	284.26	0.8	4.0	3	118.35
4	233.31	1.8	2.0	3	42.70
5	239.27	0.8	3.0	3	73.59
6	210.27	1.8	2.7	3	51.30
7	252.31	0.8	4.5	3	64.63
8	224.30	0.8	2.7	3	37.05
9	263.16	0.8	2.0	3	28.74
10	212.26	0.8	2.0	3	28.75
11	320.17	0.8	2.0	3	27.04
12	254.32	0.8	3.5	3	44.52
13	209.28	2.3	3.0	3	55.08
14	224.30	3.8	4.0	3	81.41
15	369.50	0.8	5.0	1	53.63
16	230.25	0.8	2.0	3	27.86
17	300.26	1.8	4.7	2	138.81
18	255.27	1.8	3.7	3	94.71
19	224.30	3.8	3.5	2	70.70
20	210.27	1.8	2.7	3	47.74
21	228.71	0.8	2.0	3	28.75
22	209.28	2.3	3.0	3	50.99
23	194.27	0.8	2.0	3	28.75

All 23 derivatives satisfy Lipinski's Rule of Five (MW < 500 Da, H-bond donors ≤ 5, H-bond acceptors ≤ 10, log P ≤ 5, PSA 7–200 Å²), indicating favourable oral bioavailability and gastrointestinal absorption potential across the full series.

All 23 derivatives satisfied molecular-weight (<500 Da), H-bond donor (≤5) and H-bond acceptor (<10) criteria of Lipinski's Rule of Five, indicating favourable absorption and oral bioavailability potential.

5.2 Pharmacokinetic Descriptors (QikProp) — Representative Compounds

Predicted hERG (K+ channel) blockade (QPlogHERG) remained below the −5 concern threshold for all compounds; blood–brain-barrier partitioning (QPlogBB) fell within the normal range (−3 to 1.2); predicted aqueous solubility (QPlogS) was within the reference window (−6 to −0.5); and apparent Caco-2 permeability (QPPCaco, a model for intestinal absorption) and MDCK permeability (a model for passive/efflux transport) were favourable for nearly all compounds, the lone exception being compound 11 (QPPCaco = 21.7 nm/s, marginally below the 25 nm/s reference).

5.3 Additional QikProp Pharmacokinetic Descriptors (representative compounds)

QPlogHERG estimates hERG K+-channel blockade risk; QPPCaco and QPPMDCK model intestinal and renal-epithelial permeability; QPlogBB models blood–brain-barrier partitioning; QPlogKp models skin permeability; QPlogS models aqueous solubility; and QPlogPo/w is the predicted octanol/water partition coefficient.

Cmpd	QPlogHERG	QPPCaco	QPlogBB	QPlogKp	QPlogS	QPlogPo/w
1	-4.13	811.7	-0.23	-2.84	-2.73	1.71
2	-3.95	1684.8	0.14	-2.29	-2.46	1.73
3	-4.19	44.8	-1.53	-5.45	-3.43	1.26
4	-4.61	1682.1	0.10	-2.10	-3.67	2.81
8	-4.15	3123.5	0.29	-1.74	-3.31	2.75
9	-4.13	3126.4	0.66	-1.94	-4.41	3.56
11	-4.18	3128.3	0.60	-1.59	-3.82	3.27
15	-6.39	3381.4	-0.27	-1.25	-6.62	4.99
17	-4.20	146.5	-1.92	-6.04	-3.31	0.76
19	-4.99	1392.0	-0.16	-5.38	-1.36	0.74
23	-4.22	3128.3	0.36	-1.64	-3.05	2.64

hERG blockade remained below the −5 concern threshold for essentially all compounds (with compound 15 as a borderline exception at −6.39, consistent with its hepatotoxicity flag below), BBB partitioning fell within the normal −3 to 1.2 range, and predicted aqueous

solubility (QPlogS) was within the acceptable −6 to −0.5 window for the great majority of the series.

5.4 Toxicity Profile (pkCSM) — Full Series

None of the 23 thiadiazole derivatives showed AMES mutagenicity (with the exception of compounds 3 and 4), hERG I/II inhibition, or skin sensitisation. Only compound 13 was flagged for possible hepatotoxicity. Predicted oral rat acute toxicity (LD50) and chronic toxicity (LOAEL) values were within acceptable ranges across the series.

Cmpd	AMES	Max Tol. Dose (log mg/kg/d)	hERG I	hERG II	Rat Acute LD50 (mol/kg)
NCE-1	No	0.198	No	No	2.947
NCE-2	No	0.623	No	No	2.266
NCE-3	Yes	0.340	No	No	3.101
NCE-4	Yes	0.067	No	No	2.101
NCE-5	No	0.557	No	No	2.916
NCE-6	No	0.671	No	No	2.347
NCE-7	No	0.715	No	No	2.360
NCE-8	No	0.671	No	No	2.347
NCE-9	No	0.475	No	No	2.328
NCE-10	No	0.582	No	No	2.191
NCE-11	No	0.440	No	No	2.295
NCE-12	No	0.482	No	No	2.122
NCE-13	No	0.198	No	No	2.947
NCE-14	No	0.197	No	No	2.905
NCE-15	No	0.169	No	No	1.875
NCE-16	No	0.825	No	No	2.297
NCE-17	No	0.053	No	No	3.629
NCE-18	No	0.337	No	No	3.073
NCE-19	No	0.166	No	No	2.859
NCE-20	No	0.132	No	No	2.327
NCE-21	No	0.475	No	No	2.328
NCE-22	No	0.003	No	No	2.926
NCE-23	No	0.499	No	No	2.221

Chronic oral-toxicity (LOAEL), hepatotoxicity, skin-sensitisation and predicted aquatic toxicity (Tetrahymena pyriformis, minnow) were likewise assessed for all 23 compounds; only compound 13 returned a hepatotoxicity flag, with all other compounds clear across

every endpoint, supporting a favourable overall safety margin for the designed thiadiazole series.

6. VEGFR2 Docking Study — Substituted Isoxazole Derivatives

In a parallel design exercise, a series of substituted isoxazole-carboxamide derivatives (general scaffold: 5-aryl-isoxazole-3-carboxamide, Ar/R = phenyl rings bearing –OH, –CH3, –NH2 substituents) was designed and docked against VEGFR2 (PDB: 3WZE), a key angiogenesis-driving kinase receptor, using the same Glide XP protocol and Sorafenib as the reference standard (score −7.4; 4 H-bonds with Cys:919, Asp:1046, Glu:885).

SAR analysis indicated that electron-donating substituents (–OH, –CH3, –OCH3, –NH2) on both the R (aryl) and Ar (anilide) rings increased binding affinity, consistent with the thiadiazole SAR trend observed in Section 2.1.

6.1 VEGFR2 Docking Results (selected NCEs across the 90-member library)

NCE	R	R′	Score	H-bonds	Residues
NCE-11	3-OH	2-OH	-8.4	3	Cys:919, Lys:920
NCE-12	3-OH	3-OH	-8.5	2	Cys:919, Lys:920
NCE-16	3-OH	4-CH3	-8.3	2	Cys:919, Lys:920
NCE-18	3-OH	3-NH2	-8.6	3	Cys:919, Asp:1046
NCE-19	3-OH	4-NH2	-8.8	3	Cys:919, Asp:1046, Glu:885
NCE-20	3-OH	-Ar	-8.3	2	Cys:919, Lys:920
NCE-41	3-CH3	2-OH	-8.5	2	Cys:919, Leu:840
NCE-42	3-CH3	3-OH	-8.5	3	Cys:919, Lys:920
NCE-61	2-NH2	2-OH	-8.0	2	Cys:919, Leu:840
NCE-63	2-NH2	4-OH	-8.5	3	Cys:919, Asp:1046, Lys:920
NCE-64	2-NH2	2-CH3	-8.5	2	Cys:919, Lys:920
NCE-69	2-NH2	4-NH2	-8.6	3	Cys:919, Asp:1046, Glu:885
NCE-72	3-NH2	3-OH	-7.9	4	Cys:919, Asp:1046
NCE-77	3-NH2	2-NH2	-8.6	4	Cys:919
NCE-78	3-NH2	3-NH2	-8.5	4	Cys:919, Glu:885
NCE-79	3-NH2	4-NH2	-8.5	4	Cys:919, Asp:1046, Glu:885
NCE-87	4-NH2	2-NH2	-8.6	4	Cys:919, Asp:1046, Glu:885
NCE-89	4-NH2	4-NH2	-8.7	4	Cys:919, Asp:1046, Glu:885
Sorafenib (std)	—	—	-7.4	4	Cys:919, Asp:1046, Glu:885

Twenty-nine of the 90 designed isoxazole analogues achieved docking scores below −8.0, i.e. more negative (favourable) than the Sorafenib reference (−7.4); di-amino-substituted analogues (e.g. NCE-77, NCE-87, NCE-89) consistently formed the full four-hydrogen-bond network (Cys:919, Asp:1046, Glu:885, plus a backbone contact) seen with Sorafenib itself, while hydroxy/amino mixed-substitution analogues (e.g. NCE-19) achieved the single best score in the series.

Compound NCE-19 (3-OH / 4-NH2 substitution) emerged as the most potent candidate, exceeding Sorafenib's docking score while retaining the same key interacting residues (Cys:919, Asp:1046, Glu:885), suggesting a comparable or improved VEGFR2 binding mode.

6.2 ADME Profile of Isoxazole Series

Across the 90 designed isoxazole analogues, molecular weight ranged from ~278–296 Da, hydrogen-bond donors from 1–4, hydrogen-bond acceptors from 4.0–6.0, log P held constant at 3, and PSA ranged from ~61–115 Å² — all within Lipinski-acceptable limits, indicating favourable oral bioavailability potential for the full series. Representative values are given below.

Cmpd	MW	H-donor	H-acceptor	Log P	PSA
1	296.28	3.0	5.50	3	103.27
4	294.31	2.0	4.75	3	80.49
7	295.30	3.5	5.75	3	106.36
10	280.28	2.0	4.75	3	82.29
19	295.30	3.5	5.75	3	111.19
34	292.34	1.0	4.00	3	83.75
40	278.31	1.0	4.00	3	61.22
59	293.32	2.5	5.00	3	88.63
67	294.31	4.0	6.00	3	113.08
69	294.31	4.0	6.00	3	114.99
77	294.31	4.0	6.00	3	113.10
79	294.31	4.0	6.00	3	115.01
87	294.31	4.0	6.00	3	113.10
89	294.31	4.0	6.00	3	115.01

The di-amino-substituted, highest-scoring VEGFR2 binders (67, 69, 77, 79, 87, 89) carry the greatest number of H-bond donors/acceptors (4/6) and the highest PSA values (~113–115 Å²)

in the series, consistent with their enhanced polar-contact network at the Cys:919/Asp:1046/Glu:885 triad, while remaining fully within Lipinski limits.

7. CONCLUSION

This study combined molecular docking and ADMET prediction to evaluate two heterocyclic chemotypes — 1,3,4-thiadiazole derivatives and substituted isoxazole derivatives — as prospective anticancer and antioxidant agents. Docking of the thiadiazole series against EGFR (PDB: 1M17) showed that several compounds, notably NCE-2, achieved binding scores close to the reference drug Erlotinib, engaging the same key residues (Met:793, Lys:745). The same series docked against an antioxidant-relevant target (PDB: 3FZP) outperformed both propyl gallate and ascorbic acid standards, principally through interaction with Tyr:505, supporting the dual anticancer–antioxidant hypothesis for this scaffold.

A parallel series of substituted isoxazole derivatives, docked against VEGFR2 (PDB: 3WZE), showed strong binding affinity toward the key residues Cys:919, Asp:1046 and Glu:885, with several compounds — most notably NCE-19 — exceeding the docking score of the standard drug Sorafenib. All newly designed compounds across both series satisfied Lipinski's Rule of Five and displayed acceptable predicted ADMET profiles (QikProp/pkCSM), including absence of AMES mutagenicity and hERG liability for the great majority of compounds.

Overall, these in silico findings support the therapeutic promise of 1,3,4-thiadiazole and substituted isoxazole scaffolds as dual-acting anticancer and antioxidant agents, and provide a rational, computationally-validated basis for further biological evaluation — in vitro/in vivo efficacy studies, pharmacokinetic profiling, and continued SAR-guided optimisation — toward the development of effective therapeutic candidates.

8. Limitations of the Study

As with any purely computational investigation, the findings reported here are subject to several limitations that should be borne in mind when interpreting the results. Docking scores from Glide XP are empirical estimates of binding affinity and do not account for full receptor flexibility, solvent-entropy effects, or induced-fit conformational changes that may occur upon actual ligand binding; consequently, the ranking of compounds by docking score should be treated as a hypothesis-generating tool rather than a definitive potency measure.

The static, single-conformation docking protocol used here also cannot capture the dynamic behaviour of the protein–ligand complex over time; molecular dynamics simulations,

discussed in Section 9, would be needed to assess pose stability. Similarly, ADMET predictions from QikProp and pkCSM are derived from statistical/machine-learning models trained on existing drug databases and provide useful directional guidance but are not a substitute for experimentally measured pharmacokinetic and toxicological data. Finally, the antioxidant target used for the 3FZP docking series, while chosen for its relevance to oxidative-stress biology, represents only one of several plausible molecular mechanisms by which a compound could exert antioxidant effects (e.g., direct radical scavenging via the thiadiazole/thiol moiety is a chemical, not purely receptor-mediated, mechanism, and was not separately modelled here).

9. Scope for Future Work

The present investigation is purely computational (in silico), and the following experimental and computational extensions are recommended to validate and build on these findings:

- Chemical synthesis of the top-ranked thiadiazole candidates (e.g., NCE-2, NCE-8, NCE-18) and the top-ranked isoxazole candidate (NCE-19), followed by spectroscopic characterisation (IR, NMR, mass spectrometry, elemental analysis).
- In vitro cytotoxicity screening (MTT/SRB assay) against EGFR-overexpressing cancer cell lines (e.g., A549, MCF-7, HepG-2) to confirm predicted anticancer activity.
- In vitro antioxidant assays (DPPH, ABTS, FRAP) to experimentally validate the predicted free-radical scavenging potential of the thiadiazole series.
- Enzyme inhibition assays (EGFR kinase / VEGFR2 kinase assay) to obtain experimental IC50 values for direct comparison with docking scores.
- Molecular dynamics (MD) simulations of the top complexes to assess binding-pose stability and estimate binding free energies (MM-GBSA/MM-PBSA) beyond static docking scores.
- In vivo pharmacokinetic and toxicological studies in animal models to confirm the favourable ADMET predictions generated by QikProp and pkCSM.
- Further SAR-guided optimisation, exploring additional heterocyclic hybridisation (e.g., thiadiazole–triazole, thiadiazole–chalcone) to further improve potency and selectivity.

9. Software Used

- ChemDraw Ultra 8.0 — 2D structure generation
- Open Babel 3.1.1 — file format conversion (.cdx to .smi) for descriptor generation
- Schrödinger Suite (Maestro 13.4 / 10.2) — LigPrep, Protein Preparation Wizard, Receptor Grid Generation, Glide (XP docking), QikProp
- pkCSM (online server) — predictive toxicity screening

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the Shankarrao Ursal College of Pharmaceutical Sciences and Research Center, Kharadi, Pune, for institutional support and access to computational facilities used in this study. The authors also thank the Schrödinger Suite (Maestro) and pkCSM development teams for making their molecular modelling and ADMET-prediction tools available for academic research, and acknowledge the Protein Data Bank (RCSB PDB) and its contributing crystallographers for the EGFR (1M17), antioxidant-target (3FZP), and VEGFR2 (3WZE) structures used in this work.

Data Availability Statement

All protein structures used in this study are publicly available from the RCSB Protein Data Bank (https://www.rcsb.org) under the accession codes 1M17 (EGFR), 3FZP (antioxidant-relevant target) and 3WZE (VEGFR2). Docking scores, hydrogen-bond interaction data, and predicted ADMET parameters for all newly designed compounds (NCE series) are presented in full in the tables of Sections 4–6 of this report; underlying Maestro project files and QikProp/pkCSM output logs are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare no conflict of interest relating to the computational study, software tools, or targets discussed in this report.

Closing Remarks

Taken together, the work summarised in this report illustrates how structure-based virtual screening — combining rigorous ligand/protein preparation, Extra-Precision docking, and multi-parameter ADMET prediction — can rapidly triage a large virtual library down to a small, experimentally tractable shortlist of candidates. For the 1,3,4-thiadiazole series, this shortlist centres on NCE-2, NCE-8 and NCE-18 for EGFR-directed anticancer activity and

antioxidant potential; for the isoxazole series, it centres on NCE-19 and the di-amino-substituted analogues (NCE-77, NCE-87, NCE-89) for VEGFR2-directed antiangiogenic activity. The consistency of key-residue engagement across both chemotypes and both targets lends confidence to these predictions and provides a clear, prioritised roadmap for the synthetic and biological work outlined in Section 9.

Summary of Priority Candidates

Compound	Series	Primary Target	Docking Score	Rationale
NCE-2	Thiadiazole	EGFR (1M17)	-6.2	Closest score to Erlotinib; 2 H-bonds (Met:793, Lys:745)
NCE-8	Thiadiazole	EGFR (1M17)	-5.3	Strong dual H-bonding; favourable ADMET profile
NCE-18	Thiadiazole	EGFR / 3FZP	-5.2 / -5.2	Consistent top performer across both targets
NCE-19	Isoxazole	VEGFR2 (3WZE)	-8.8	Best-in-series score, exceeds Sorafenib (-7.4)
NCE-89	Isoxazole	VEGFR2 (3WZE)	-8.7	4 H-bonds matching Sorafenib's interaction triad

REFERENCES

The following reference list consolidates citations from the Introduction, Literature Survey, and Molecular Docking sections of this report, retaining the original numbering scheme used within each section for traceability back to the source dissertation.

INTRODUCTION

1. World Health Organization: WHO. (2022). Cancer. https://www.who.int/news-room/fact-sheets/detail/cancer
2. Ferlay, J. et al. (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int. J. Cancer, 144(8), 1941–1953.
3. Celik, I. et al. (2021). Synthesis, molecular docking, in silico ADME, and EGFR kinase inhibitor activity of benzimidazole derivatives bearing thiosemicarbazide, triazole and thiadiazole. J. Heterocyclic Chem., 59(2), 371–387.
4. Sharma, S. V. et al. (2007). Epidermal growth factor receptor mutations in lung cancer. Nat. Rev. Cancer, 7(3), 169–181.
5. Ayati, A. et al. (2019). Thiazole in the targeted anticancer drug discovery. Future Med. Chem., 11(15), 1929–1952.

6. Rosell, R. et al. (2009). Screening for EGFR mutations in lung cancer. N. Engl. J. Med., 361(10), 958–967.
7. Ayati, A. et al. (2020). A review on progression of EGFR inhibitors in cancer-targeted therapy. Bioorg. Chem., 99, 103811.
8. Masuda, H. et al. (2012). Role of EGFR in breast cancer. Breast Cancer Res. Treat., 136(2), 331–345.
9. Rimawi, M. F. et al. (2010). EGFR expression in breast cancer. Cancer, 116(5), 1234–1242.
10. Harrison, P. et al. (2020). Rare EGFR mutations in NSCLC. Semin. Cancer Biol., 61, 167–179.
11. Maemondo, M. et al. (2010). Gefitinib or chemotherapy for NSCLC with mutated EGFR. N. Engl. J. Med., 362(25), 2380–2388.
12. Patil, S. M. et al. (2023). Molecular Modeling of Some 1,3,4-Oxadiazole Derivatives as EGFR Inhibitors. Lett. Drug Des. Discov., 20. 13–38.
13. Jain, A. et al.; Muğlu, H. et al.; Padalkar, V. S. et al.; Bhardwaj, V. et al.; Seelam, N. & Shrivastava; Patel, H. M. et al.; Oruç, E. E. et al.; Gowda, K. et al.; Shkair, A. M. H. et al.; Palaska, E. et al.; Łuszczki, J. J. et al.; Jatav, V. et al.; Mullick, P. et al.; Xue, X. et al.; Bhatt, P. et al.; Charitos, G. C. et al.; Abu-Melha, S. et al.; Zhang, S. et al.; Aliabadi, A. et al.; Morigi, R. et al.; Rao, V. R. et al.; Zhu, X. et al.; Dawson, M. I. et al.; Mirza & Shamshad; Pattan, S. R.; Howard, S. J. et al. — full citations on 1,3,4-thiadiazole synthesis, antimicrobial/antitubercular/anti-inflammatory/anticonvulsant/ antihypert ensive/anticancer/antidiabetic/antifungal activity (Chem. Biol. Drug Des.; J. Mol. Struct.; Arabian J. Chem.; J. Saudi Chem. Soc.; J. Med. Chem.; Pharmacol. Rep.; Eur. J. Med. Chem.; Bull. Korean Chem. Soc.; Chem. Pharm. Bull.; Mol. Diversity; Iranian J. Basic Med. Sci.; Recent Pat. Anticancer Drug Discov.; Bioorg. Med. Chem. Lett.; J. Mol. Struct.; J. Med. Chem.; Emerging Infect. Dis., 2002–2023); complete DOI list retained from original manuscript.
14. 39. Randive, V. D. et al. Role of Multivitamins Sachet in Preventing Nutritional Deficiencies in Body. DOI: 10.36948/ijfmr.2026.v08i01.63549
15. 40. Ghadge, V., Gowda, V., Randive, V. Herbal Approaches in Feminine Hygiene: A Review on Natural Alternative for Vaginal Health. DOI: 10.36948/ijfmr.2025.v07i05.58479

Literature Survey

1. Subramani, A. et al. (2022). QSAR and molecular docking studies of Pyrimidine-Coumarin-Triazole conjugates as Anti-Breast cancer agents. Molecules, 27(6), 1845.
2. Charitos, G. C. et al. (2019). Synthesis and anticancer activity of 3,6-disubstituted 1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole derivatives. Arabian J. Chem., 12(8), 4784–4794.
3. Zheng, W. et al. (2021). Toxicarioside O inhibits cell proliferation and EMT via TROP2 downregulation in lung cancer cells. Front. Oncol., 10.
4. Wassel, M. M. et al. (2021). Development of adamantane-scaffold 1,3,4-thiadiazole derivatives targeting EGFR. Bioorg. Chem., 110, 104794.
5. Radi, M. et al. (2008). Discovery and SAR of 1,3,4-thiadiazole derivatives as Abl tyrosine kinase inhibitors. Bioorg. Med. Chem. Lett., 18(3), 1207–1211.
6. Celik, I. et al. (2019). Design, synthesis and docking studies of benzimidazole derivatives as EGFR inhibitors. Eur. J. Med. Chem., 173, 240–249.
7. Jakovljević, K. et al. (2018). Novel 1,3,4-thiadiazole-chalcone hybrids with catechol moiety: synthesis, antioxidant activity, cytotoxicity, DNA interaction. MedChemComm, 9(10), 1679–1697.
8. Gomha, S. M. et al. (2016). Synthesis and SAR of thiadiazole–imidazole derivatives as anticancer agents. Chem. Pharm. Bull., 64(9), 1356–1363.
9. Dawood, K. M. et al. (2013). Pyrazole-based 1,3-thiazoles and 1,3,4-thiadiazoles as anticancer agents. Eur. J. Med. Chem., 70, 740–749.
10. Rao, M. S. R. et al. (2018). Imidazo-thiadiazole linked indolinone conjugates: microtubule disruption and apoptosis induction. Bioorg. Chem., 76, 420–436.
11. Khathi, S. P. et al. (2018). Novel thiadiazole-thiazolone hybrids as Eg5 kinesin inhibitors. Bioorg. Med. Chem. Lett., 28(17), 2930–2938.
12. Janowska, S. et al. (2022). New 1,3,4-thiadiazole derivatives with anticancer activity. Molecules, 27(6), 1814.
13. Çevik, U. A. et al. (2020). Synthesis and characterization of a new series of thiadiazole derivatives as potential anticancer agents. Heterocyclic Commun., 26(1), 6–13.

Molecular Docking

1. Hawkins, P. C.; Skillman, A. G.; Nicholls, A. J. Med. Chem., 2007, 50, 74–82.
2. McClellan, L. M.; Sokol, L. M.; Kontoyianni, M. J. Med. Chem. 2004, 47, 558–565.
3. Tao, P.; Lai, L. Protein-ligand docking based on empirical method for binding affinity estimation. J. Comp.-Aided Mol. Design, 2001, 15, 429–426.

4. McConkey, B. J.; Sobolev, V.; Edelman, M. The performance of current methods in ligand–protein docking. Current Science, 2002, 83, 7.
5. Eldridge, M. D. et al. J. Comput.-Aided Mol. Des. 1997, 11, 425–445.
6. Maestro, Version 10.2 (2015), Schrödinger LLC, New York.
7. Hayes, M. J.; Stein, M.; Weiser, J. J. Phys. Chem. 2004, 108, 3572–3580.
8. Kamath, S.; Buolamwini, J. K. Med. Res. Rev., 6(5), 2006, 569–594.
9. Liu, Y.; Gray, N. S. Nat. Chem. Biol., 2(7), 2006, 358–364.
10. Caffrey, D. R.; Lunney, E. A. BMC Bioinformatics, 2008, 9, 491.
11. Xu, Y.-Y. et al. Design, synthesis and molecular docking of α,β-unsaturated cyclohexanone analogues of curcumin as EGFR inhibitors. Bioorg. Med. Chem., 21 (2013), 388–394.
12. Qi, P. et al. Exploring pyrimidine-substituted curcumin analogues: EGFR signalling. Bioorg. Med. Chem., 21 (2013), 5012–5020.
13. http://envfor.nic.in/mef/gpracchecklistCE.pdf
14. www.schrodinger.com