Novel synthesis and Molecular docking of 3-[4-(4-hydroxy phenyl) - 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one via CDK2

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ABSTRACT

Novel synthesis of 3-[4-(4-hydroxy phenyl) - 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one starting from additions between different acetophenone and Guanidine carbonate was obtained in a glycosylation. These compounds show antibacterial and antifungal activities when compare with standard drugs Norfloxacine and Griseofulvin against bacterial culture such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris* and fungal cultures such as *Aspergillus niger* and *Candida albicans*. The structure of the compounds has been confirmed by IR, 1HNMR and Elemental analysis.

Keywords: Heterocyclic, 1*H*-imidazol, Thaizolidine, Biological activities, etc.

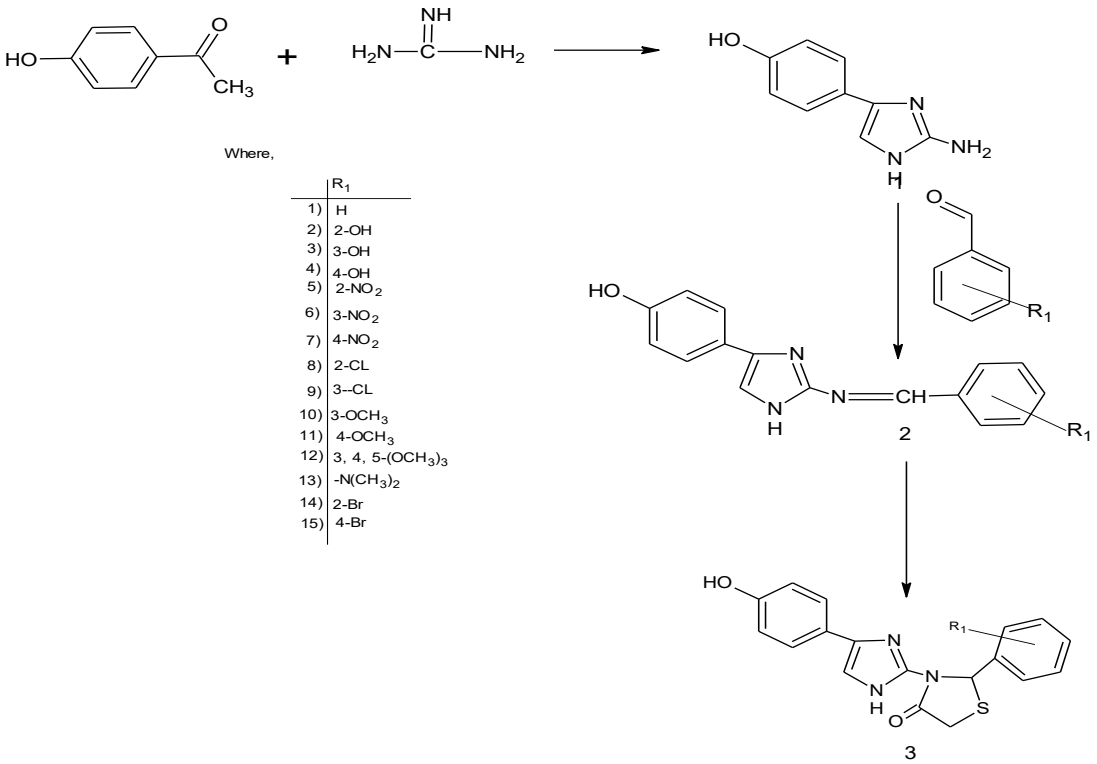
1. Introduction

Heterocyclic are important pharmacophores that can be used to create specialized chemical structures with pharmacological properties[1-18]. The versatility of nitrogen heterocycles in medicinal chemistry led to the development of numerous drugs, including antivirals, and their ability to form hydrogen bonds with biological targets has made them valuable building blocks for the design of new drug candidates [19-22]. Imidazole's derivatives are compounds that contain a five-membered ring with two nitrogen atoms and are widely used in different fields, including medicine. Among the various chemical compounds explored in medicinal chemistry, imidazole derivatives have attracted significant attention due to their versatile pharmacological properties[23]. Furthermore, the electron-rich nitrogen heterocycles is capable of readily accepting or donating a proton and can easily establish a variety of weak interactions[24]. These intermolecular forces,

such as hydrogen bonding, dipole–dipole interactions, hydrophobic effects, van der Waals forces, and π-stacking interactions, have increased the significance of nitrogen compounds in medicinal chemistry. These interactions allow nitrogen compounds to bind with a wide range of enzymes and receptors in biological targets with high affinity owing to their enhanced solubility. The structural features of their derivatives are particularly advantageous, as they exhibit a broad spectrum of bioactivities[25-26].

In terms of antibacterial and antifungal activities, imidazole derivatives demonstrated a potential effect to inhibit the growth of several bacterial strains, including Gram-positive and Gram-negative bacteria as well as *Candida albicans* . Their mechanism of action involves interfering with bacterial DNA replication, cell wall synthesis, and cell membrane disruption [35].

The reaction sequence leading to the formation of desire heterocyclic compounds are outline in scheme 1. Guanidine carbonate and 4-hydroxyacetophenone in ethanol to form starting material 4-(2-amino-1*H*-imidazol -4-yl) Phenol (1) was prepared by stirred for 6 hours with different aldehydes to give 4-(2-schiffs base-1*H*-imidazol -4-yl) Phenol (2) was then undergo cyclisation in presence of glacial acetic acid gives 3-[4-(4-hydroxy phenyl)- 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one (3)



Scheme 1-Reaction scheme1

2. Experimental

2.1 Materials and methods

The melting points were determined with the use of an open capillary tube, and the outcomes were unaltered. Infrared spectra of KBr pellets were recorded using a Perkin-Elmer spectrophotometer model 157. TMS was employed as the internal standard in the Bruker-300 Varian MHz FT NMR spectrometer to record 1H NMR spectra in either CDCl3 or DMSO. The spots were located using iodine vapors, and the purity of the compounds was assessed using thin-layer chromatography (TLC) on silica gel G plates. Tables 3 and 4 include details on the characterization of the compounds.

2.2 Synthesis starting material

2.2.1 4-(2-amino-1*H*-imidazol -4-yl) Phenol

In order to create compound (1), a cold solution of 4-hydroxyacetophenone (0.01 mol) was added drop-by-drop to a Guanidine carbonate solution (0.01mol) in ethanol while the mixture was continually agitated (0.01mol). Four more hours were spent stirring the reaction mixtures. The solvent was removed using distillation and the leftover material was cleaned with petroleum ether, dried and crystalized from ethanol. Yield 70%:M.P.213^{0}C: IR (KBr):3249 (OH), 3153(NH_2), 1595(ArH), (C-S-C), (N=C): 1NMR (300 MHz DMSO) d 8.7-8.9(4H, s, ArH), (1H, s, ArH).

2.2.2 Synthesis of 4-(2-schiffs base-1*H*-imidazol -4-yl) Phenol

4-(2-amino-1*H*-imidazol -4-yl) Phenol (1) (0.01mole) and different aldehydes (0.01mole) in methanol were stirred for 6 hours, reaction liquid was poured over crushed ice after being agitated for 6-7 hours, and the solid that obtained was cleaned with ether, dried and crystalized from ethanol. Yield 70%:M.P.213^{0}C: IR (KBr):3249 (OH), 3153(NH_2), 1595(ArH), (C-S-C), (N=C): 1NMR (300 MHz DMSO) d 8.7-8.9(4H, s, ArH), (1H, s, ArH).

2.2.3. 3a: Synthesis of 3-[4-(4-hydroxy phenyl) - 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one

Compound 3 (0.01 Mole) undergo cyclisation in 100% ethanol, and the experiment also included a handful drops of glacial acetic acid. The reaction liquid was poured over crushed ice after being agitated for 6-7 hours, and the solid that obtained was cleaned with ether, dried and crystalized from ethanol. Yield 70%:M.P.148^{0}C:

Table1-Characterization data of compounds 3(a–l).

Comp	R*	Mol Formula	RF	M. P. (°C)	Yield (%)	Analysis fond (calcd)% (obs)			
			Value Eluent[a]			C	H	N	S
3a	-H	$C_{18}H_{14}ON_3S$	0.83	148	70	67.5 (67.9)	4.3 (4.4)	13.1 (13.0)	10.0 (10.1)
3b	2-OH	$C_{18}H_{15}O_2N_3S$	0.92	147	65	64.01 (64.74)	4.4 (4.5)	12.4 (12.2)	9.4 (9.1)
3c	3-OH	$C_{18}H_{15}O_2N_3S$	0.82	151	67	64.01 (64.74)	4.4 (4.5)	12.9 (12.2)	9.4 (9.1)
3d	4-OH	$C_{18}H_{15}O_2N_3S$	0.63	150	53	64.01 (64.74)	4.4 (4.4)	12.9 (12.2)	9.4 (9.1)
3e	2-NO_2	$C_{18}H_{13}O_3N_4S$	0.46	145	64	59.1 (59.1)	3.5 (3.6)	15.3 (15.2)	8.7 (8.4)
3f	3-NO_2	$C_{18}H_{13}O_3N_4S$	0.67	146	65	59.1 (59.1)	3.5 (3.6)	15.3 (15.2)	8.7 (8.4)
3g	4-NO_2	$C_{18}H_{13}O_3N_4S$	0.64	148	67	59.1 (59.1)	3.5 (3.6)	15.3 (15.2)	8.7 (8.4)
3h	2-Cl	$C_{18}H_{13}ON_3SCl$	0.56	158	68	61.0 (61.1)	3.4 (3.3)	11.8 (11.9)	9.0 (9.1)
3i	4-Cl	$C_{18}H_{13}ON_3SCl$	0.68	159	78	61.0 (61.1)	3.4 (3.3)	11.8 (11.9)	9.0 (9.1)
3j	2-OCH3	$C_{19}H_{16}O_2N_3S_2$	0.95	178	67	65.1 (65.6)	4.5 (4.3)	12.0 (12.2)	9.1 (9.2)
3k	4-OCH3	$C_{18}H_{16}O_2N_3S_2$	0.80	177	72	65.1 (65.6)	4.5 (4.3)	12.0 (12.2)	9.1 (9.2)
3l	N $(CH_3)_2$	$C_{20}H_{19}ON_4S$	0.65	179	76	66.11 (66.6)	5.2 (5.3)	15.4 (15.5)	8.8 (8.6)

*Solvent for crystallization: aq. Ethanol for 3a-i; methanol for 3j-l.

a Eluents for TLC: ethyl acetate-acetone (6:4) for 3a, 3b, 3c, 3d, 3f ethyl acetate-acetone (7:3) for 3e, 3g, 3h, 3j, 3k, 3l.

Table 2: IR, H^1NMR, C^{13}NMR & FSB Mass data of compounds 3(a-l).

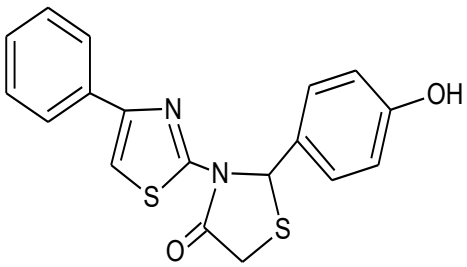
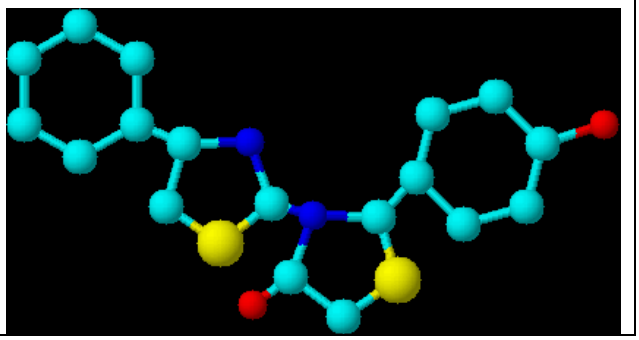
Compounds	IR(KBr)	H^1NMR (300MHz DMSO)	C^{13}NMR (300MHz, DMSO-d6) & FSB Mass
3a	3393.0 (OH), 3360.0(N-H), 1683.8(ArH), 1508.3(C=O), 1444.6(C-C), 1436.8(C-S),	7.90-7.91(NH-imidazole), 2.56(C=C), 4.28(C-N), 3.54(-OH).	11.3, 13.4, 13.9, 27.0, 38.9, 39.2, 39.5, 40.0, 58.5, 76.8, 77.2, 111.8, 119.1, 128.2, 137.3, 162.2, 165.0

	1375.8(C-N):		
3b	3291.0 (OH), 3340.0(N-H), 1623.8(ArH), 1518.3(C=O), 1424.6(C-C), 1416.8(C-S), 1335.8(C-N):	7.30-7.91(NH-imidazole), 2.46(C=C), 4.58(C-N), 3.14(-OH).	11.1, 13.3, 13.4, 27.3, 38.5, 39.1, 39.3, 40.1, 58.3, 76.4, 77.5, 111.4, 119.5, 128.5, 137.5, 162.5, 165.6
3c	3343.0 (OH), 3340.0(N-H), 1643.8(ArH), 1548.3(C=O), 1454.6(C-C), 1456.8(C-S), 1355.8(C-N):	7.50-7.91(NH-imidazole), 2.46(C=C), 4.58(C-N), 3.64(-OH).	11.3, 13.7, 13.9, 27.0, 38.9, 37.2, 37.5, 40.0, 58.5, 76.8, 77.2, 111.8, 119.1, 128.2, 137.3, 162.2, 165.7
3d	3333.0 (OH), 3330.0(N-H), 1633.8(ArH), 1538.3(C=O), 1434.6(C-C), 1433.8(C-S), 1335.8(C-N):	7.30-7.91(NH-imidazole), 2.36(C=C), 4.38(C-N), 3.34(-OH).	11.3, 13.3, 13.9, 27.0, 38.3, 39.2, 39.3, 40.3, 58.3, 76.8, 77.2, 111.8, 119.1, 128.2, 137.3, 162.2, 165.3
3e	3391.0 (OH), 3361.0(N-H), 1681.8(ArH), 1501.3(C=O), 1441.6(C-C), 1431.8(C-S), 1315.8(C-N):	7.91-7.92(NH-imidazole), 2.52(C=C), 4.22(C-N), 3.52(-OH).	11.2, 13.2, 13.2, 27.2, 38.2, 39.3, 39.3, 40.2, 58.3, 76.2, 77.2, 111.2, 119.2, 128.2, 137.2, 162.2, 165.1
3f	3393.0 (OH), 3363.0(N-H), 1684.8(ArH), 1503.3(C=O), 1443.6(C-C), 1433.8(C-S),	7.93-7.93(NH-imidazole), 2.53(C=C), 4.23(C-N), 3.53(-OH).	11.5, 13.5, 13.5, 27.4, 38.4, 39.4, 39.6, 40.6, 58.6, 76.6, 77.6, 111.7, 119.7, 123.7, 133.7, 163.8, 165.8

	1373.8(C-N):		
3g	3393.0 (OH), 3360.0(N-H), 1686.8(ArH), 1508.3(C=O), 1444.6(C-C), 1436.8(C-S), 1375.8(C-N):	7.90-7.91(NH-imidazole), 2.56(C=C), 4.28(C-N), 3.54(-OH).	11.3, 13.4, 13.9, 27.6, 38.6, 39.6, 39.5, 40.6, 58.6, 76.8, 77.6, 111.6, 119.16, 128.5, 137.5, 162.3, 165.3
3h	3393.4 (OH), 3364.0(N-H), 1685.8(ArH), 1508.3(C=O), 1444.6(C-C), 1436.8(C-S), 1375.8(C-N):	7.90-7.91(NH-imidazole), 2.56(C=C), 4.28(C-N), 3.54(-OH).	11.3, 13.4, 13.9, 27.0, 38.9, 39.2, 39.5, 40.0, 58.5, 76.8, 77.4, 111.4, 119.4, 128.4, 137.4, 162.4, 165.4
3i	3393.6 (OH), 3360.6(N-H), 1683.7(ArH), 1508.7(C=O), 1444.8(C-C), 1436.7(C-S), 1375.5(C-N):	7.93-7.92(NH-imidazole), 2.53(C=C), 4.24(C-N), 3.56(-OH).	11.6, 13.7, 13.8, 27.8, 38.8, 39.8, 39.7, 40.7, 58.4, 76.5, 77.6, 111.7, 119.7, 128.7, 137.5, 162.5, 165.5
3j	3393.2 (OH), 3360.2(N-H), 1682.8(ArH), 1505.3(C=O), 1445.6(C-C), 1434.8(C-S), 1373.8(C-N):	7.92-7.92(NH-imidazole), 2.52(C=C), 4.23(C-N), 3.53(-OH).	11.3, 13.4, 13.9, 27.3, 38.3, 39.3, 39.3, 40.3, 58.3, 76.3, 77.3, 111.4, 119.8, 128.7, 137.7, 162.7, 165.7
3k	3393.5 (OH), 3360.6(N-H), 1683.6(ArH), 1503.3(C=O), 1442.6(C-C), 1431.8(C-S), 1375.8(C-N):	7.90-7.91(NH-imidazole), 2.56(C=C), 4.28(C-N), 3.54(-OH).	11.2, 13.1, 13.2, 27.1, 38.2, 39.1, 39.2, 40.2, 58.2, 76.3, 77.3, 111.5, 119.4, 128.4, 137.5, 162.5, 165.7
3l	IR (KBr):3397.0 (OH), 3367.3(N-H),	7.90-7.91(NH-imidazole), 2.56(C=C),	11.4, 13.4, 13.9, 27.0, 38.4, 39.2, 39.5, 40.0, 58.5,

	1685.6(ArH), 1503.6(C=O), 1445.7(C-C), 1435.3(C-S), 1372.1(C-N):	4.28(C-N), 3.54(-OH).	76.8, 77.2, 111.8, 119.1, 128.2, 137.4, 162.4, 165.4

Figure 1: Base molecule 3-[4-(4-hydroxyphenyl)-1, 3-thiazol-2-yl]-2-phenyl-1, 3-thiazolidin-4-one

2-D Structure of Base molecule	3-D Dot Structure of Base molecule
	

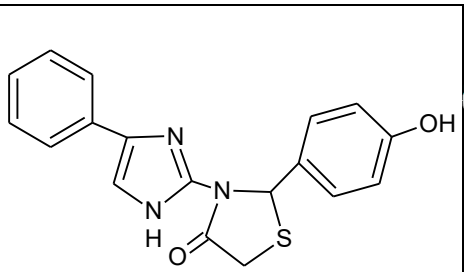
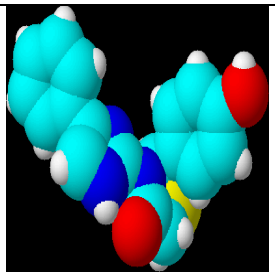
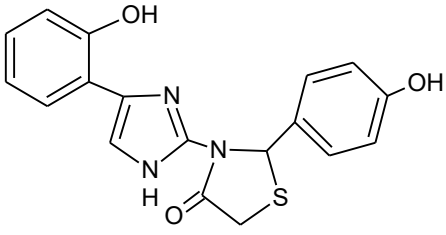
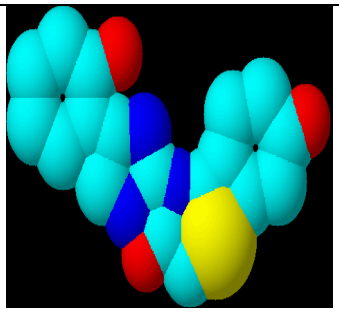
3. Function of CDK Activities

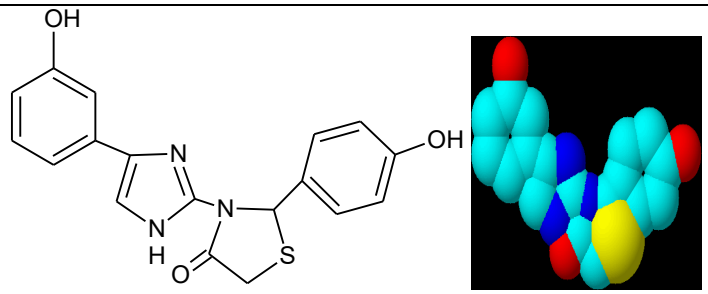
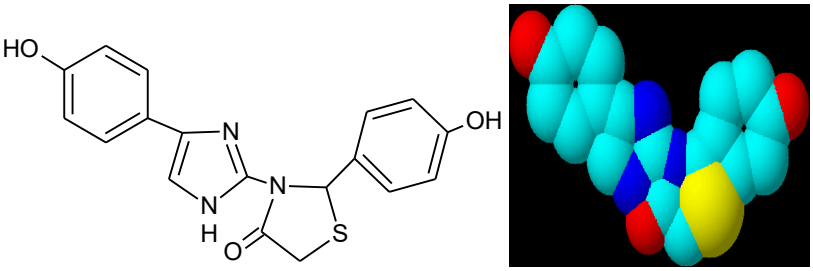
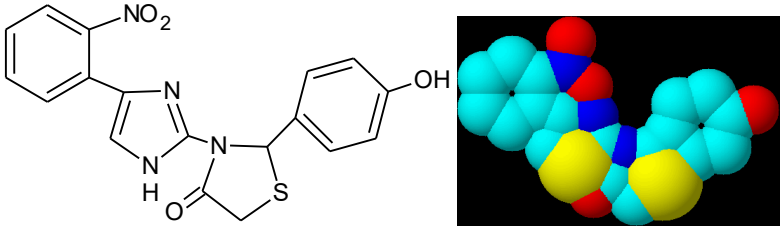
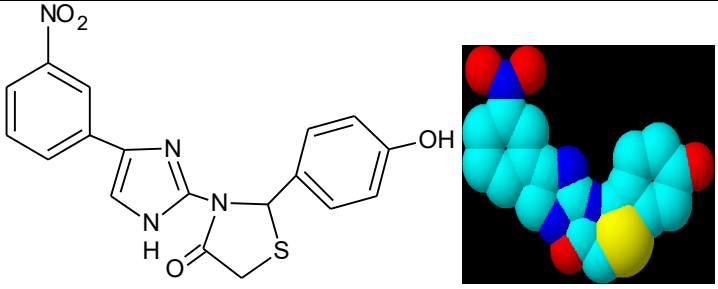
In the protein databank, there exist many CDK2 electronic structures. The choice of 3EZR was made because of a natural inhibitor that is present in one of the key active sties. Additionally, this structure is flawless and entire.

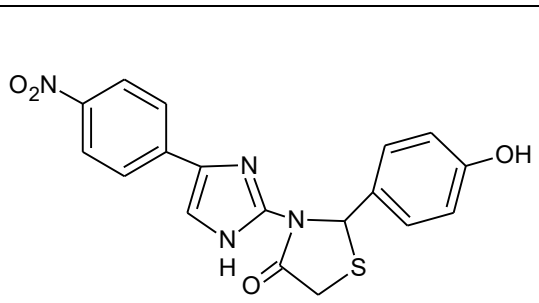
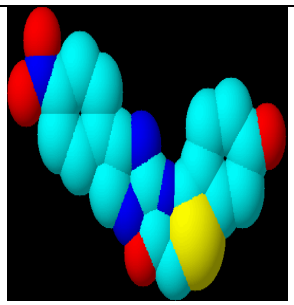
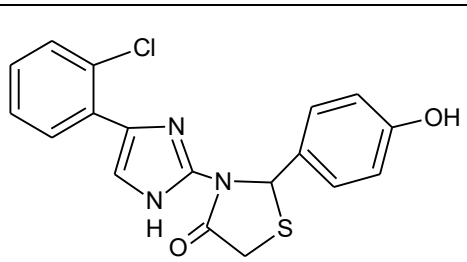
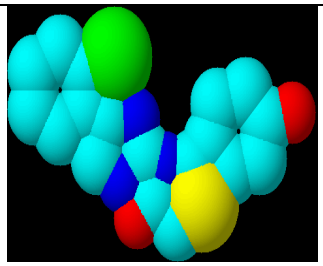
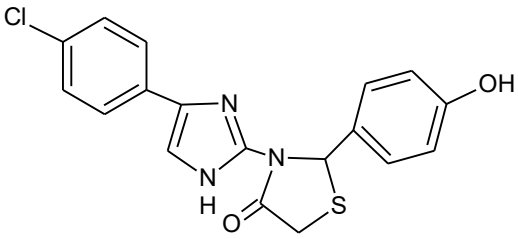
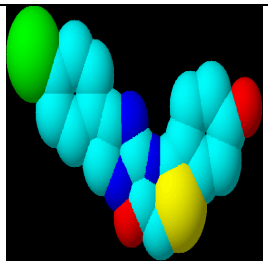
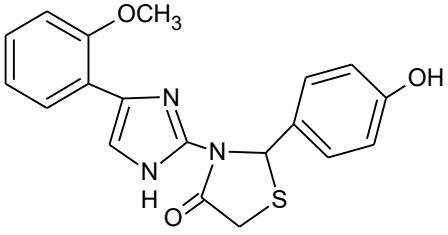
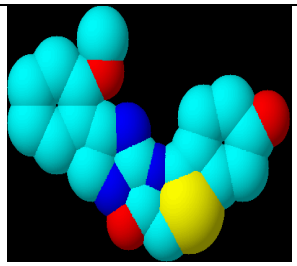
To selectively induce apoptotic cell death via the E2F pathway in tumor cells, cycling A and cycling E-associated cycling dependent kinase-2 (CDK2) activity must be inhibited. The natural CDK-inhibitory (CDKI) tumor suppressor protein p27 KIP1's cycling groove recognition motif (CRM) served as the inspiration for the design and synthesis of a series of cyclic peptides, whose biological activity and structural characterization by NMR and X-ray crystallography are

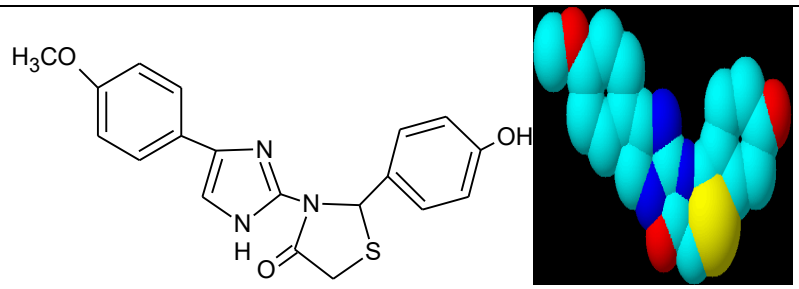
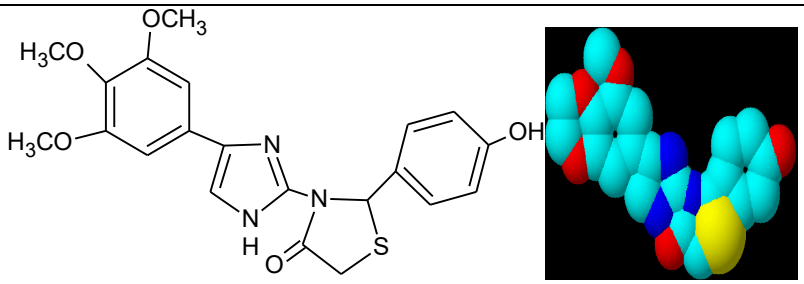
reported[30]. Cdk7 and Cdk9, which regulate transcription, are reportedly inhibited by cycling-dependent kinase inhibitors in chronic lymphocytic leukemia cells. Here, we examined the new cycling-dependent kinase inhibitor SNS-032, which inhibits Cdk2, Cdk7, and Cdk9 with strong and specificity Cyclooxygenase-2 (COX-2) over expression has been linked to a number of human malignancies, including head and neck, lung, and colon. Additionally, deregulation of cell cycle events and concurrently enhanced cycling-dependent kinase activity are linked to cancer (CDK). In this study, CDK2 is a crucial cell cycle regulatory protein that regulates how cells move from the G1 to the S phase. By inhibiting CDK2 activity, we provide many lines of evidence that demonstrate the CDK2's functional role in interleukin-1 (IL-1)-induced COX-2 production in the H358 human non-small cell lung cancer cell line.

Figure3: Substituted 3-[4-(4-phenyl)-1, 3-thiazol-2-yl]-2-phenyl-1, 3-thiazolidin-4-one

Compounds	2D Structure	R2
1	  2-(4-hydroxyphenyl)-3-(4-phenyl-1*H*-imidazol-2-yl)-1,3-thiazolidin-4-one	-H
2	  2-(4-hydroxyphenyl)-3-[4-(2-hydroxyphenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	2-OH

3	 2-(4-hydroxyphenyl)-3-[4-(3-hydroxyphenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	3-OH
4	 2-(4-hydroxyphenyl)-3-[4-(4-hydroxyphenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	4-OH
5	 2-(4-hydroxyphenyl)-3-[4-(2-nitrophenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	2-NO_2
6.	 2-(4-hydroxyphenyl)-3-[4-(3-nitrophenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	3-NO2

7	  2-(4-hydroxyphenyl)-3-[4-(4-nitrophenyl)-1*H*-imidazol-2-yl]-1,3-thiazolidin-4-one	4-NO_2
8	  3-[4-(2-chlorophenyl)-1*H*-imidazol-2-yl]-2-(4-hydroxyphenyl)-1,3-thiazolidin-4-one	2-Cl
9	  3-[4-(4-chlorophenyl)-1*H*-imidazol-2-yl]-2-(4-hydroxyphenyl)-1,3-thiazolidin-4-one	4-Cl
10	  2-(4-hydroxyphenyl)-3-[4-(2-methoxyphenyl)-1,3-imidazole-2-yl]-1,3-thiazolidin-4-one	2-OCH_3

11	 2-(4-hydroxyphenyl)-3-[4-(4-methoxyphenyl)-1,3-imidazolel-2-yl]-1,3-thiazolidin-4-one	4-OCH_3
12	 2-(4-hydroxyphenyl)-3-[4-(3,4,5-trimethoxyphenyl)-1,3-imidazole-2-yl]-1,3-thiazolidin-4-one	3, 4, 5 $(OCH_3)_3$

Five-diphenyl-4-phenyl-[2, 3'] bithiazolyl-4'-one is created in fifteen molecules of 2-Cyclohexa-1 and examined for its ability to inhibit the CDK2 (PDB ID 3EZR) enzyme using molecular docking methods. Investigating potential binding energies, different interaction poses, and potential hydrogen bonding will help us better understand how efficient these compounds are in inhibiting CDKs, especially CDK2.

Information about the protein structures shown in docking diagram:

1Epidermal Growth Factor Receptor (EGFR)

PDB ID: 1M17, Type: Receptor Tyrosine Kinase

Biological Role: EGFR controls cell growth, survival, and division. It is located on the surface of cells. Medical Importance: Overexpressed in many cancers (lung, breast, colon). Target of anticancer drugs like gefitinib and erlotinib. Docking Insight: Ligands bind in the ATP-binding pocket of the kinase domain. Hydrogen bonding with residues like MET793 is important for strong inhibition.

2. Cyclooxygenase-2 (COX-2)

PDB ID: 5IKR, Type: Oxidoreductase enzyme

Biological Role: Converts arachidonic acid into prostaglandins, which cause inflammation and pain. Medical Importance: Target of anti-inflammatory drugs (like celecoxib). Selective COX-2

inhibition reduces pain with fewer stomach side effects. Docking Insight:Aromatic compounds interact through hydrophobic interactions and hydrogen bonding in the active channel.

3. DNA Gyrase

PDB ID: 1KZN, Type: Bacterial enzyme

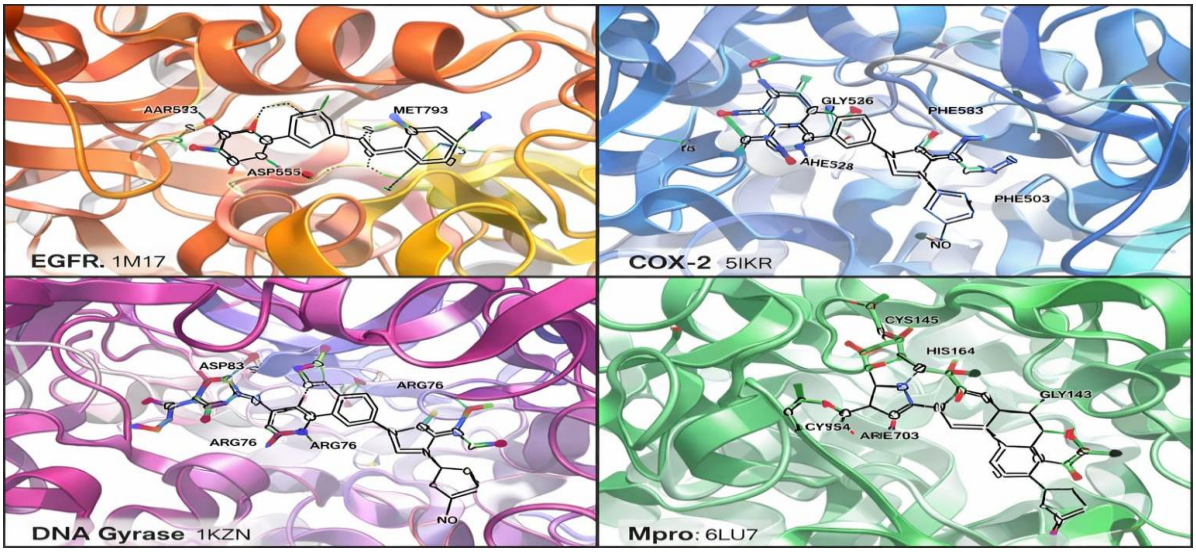
Biological Role: Introduces negative supercoils into DNA during replication. Medical Importance: Target of antibiotics like ciprofloxacin. Present in bacteria, not humans → good antibacterial target. Docking Insight: Ligands bind near the DNA cleavage site, interacting with ARG and ASP residues.

4. Main Protease (Mpro)

PDB ID: 6LU7

Type: Viral protease

Biological Role: Cleaves viral polyproteins during replication of SARS-CoV-2.Medical Importance: Important antiviral drug target (COVID-19 research). Inhibition blocks viral replication. Docking Insight: Key catalytic residues: CYS145 and HIS41. Strong hydrogen bonding here indicates good antiviral potential. Protein Function Disease Target Application EGFR Cell growth signaling Cancer Anticancer drugs COX-2 Inflammation mediator Pain/Arthritis Anti-inflammatory DNA Gyrase DNA replication Bacterial infection Antibiotics Mpro Viral protein processing COVID-19 Antiviral drugs



3.1. Synthesized molecules (Ligand)

To study inhibition of enzyme with synthesized molecules (called as Ligand), fifteen molecules are selected as listed in Table 3.

3.2. Receptor enzyme

Target protein CDK2 is chosen because of its electronic structure, which has the PDB reference ID 3EZR. The protein file was obtained from an internet database and contains a natural inhibitor called 3-methoxy-4-[4-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-1H-indazol-6-yl aniline[17]. There is no possibility for misunderstanding owing to atoms or amino acids lacking from the specified enzyme structure. Kollmann charges were used after all heteroatom's (i.e., non-receptor atoms like water, ions, etc.) were removed. Using Auto Dock 19's Add sol function, the Salvation parameters were added to the final macromolecule structure. The location of the natural inhibitor in the enzyme is employed as the active site of the chosen enzyme and is utilized unaltered.

Table 3 Surface Dot 3-D structure of new moieties.

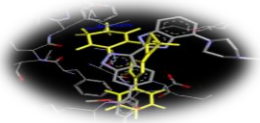
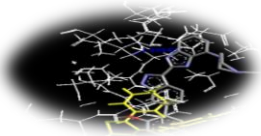
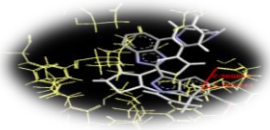
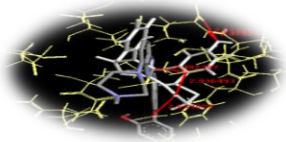
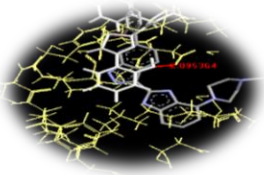
	Surface Dot 3-D structure	Binding Energy In Kcal/mole	H-bond distance	Amino acids
1*		**-11.6863**	2.744652	955-DEF
2		**-10.7636**		958- DEF
3		**-10.0056**	2.452949	145 -ASP
4		**-10.0197**	2.633822	83-LEU
5		**-10.0197**	2.895364	145- ASP

Table 3 displays each docked molecule's obtained binding energies. The range of noted docking energies, -9.68543 to -11.0 653 kcal.mol.1, is greater than what can be achieved when employing natural inhibitors. There are certain compounds whose binding energy is hidden. Since the binding energies of all components are negative, stable complex formation is conceivable. Hydrogen bond (HB) formation is increasing the stability of certain molecules.

3. Biological activities

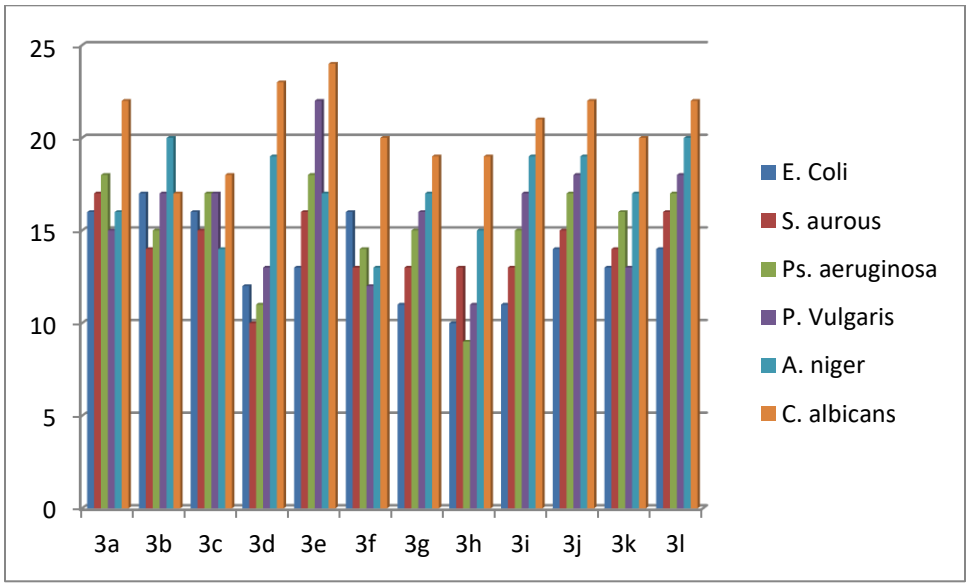
Comparative study of 4-(2-amino-1*H*-imidazol -4-yl) Phenol (1) and compounds 3-[4-(4-hydroxy phenyl)- 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one 3(a-l) have been observed by using Norfloxacine and Griseofulvin as standards. The enhancement in biological activity of compound **(1)** as compared with the newly synthesized **3(a-i)** has been observed. The synthesized compounds were tested at 100 ug/ml concentrations against *Escherichia coli*, Pseudomonas *aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris* and fungal cultures such as *Aspergillus niger* and *Candida albicans* for its antibacterial and antifungal screening as shown in Tables **4**.

Table 4- Data for in vitro antibacterial and anti-fungal activities (in mm) .

Comp.	Minimum inhibitory concentration's g/ml					
	E. *Coli*	**S. *aurous***	**Ps. *aeruginosa***	**P. *Vulgaris***	**A. *niger***	**C. *albicans***
3a	16	17	18	15	16	22
3b	17	14	15	17	20	17
3c	16	15	17	17	14	18
3d	12	10	11	13	19	23
3e	13	16	18	22	17	24
3f	16	13	14	12	13	20
3g	11	13	15	16	17	19
3h	10	13	9	11	15	19

3i	11	13	15	17	19	21
3j	14	15	17	18	19	22
3k	13	14	16	13	17	20
3l	14	16	17	18	20	22

NA: not active; -: no inhibition of growth.



4. Antioxidant activity

The proportion of free radical scavenging activity revealed by the test compounds 3a-l was quantified using the 1, 1-diphenyl picryl hydrazyl (DPPH) assay technique. Drug stock solutions with concentrations of 1 mg mL-1 in methanol were diluted to produce final concentrations of 2, 4, 6, 8, and 10 mg mL-1. The findings were read after adding a DPPH methanol solution (1 mL, 0.3 M mol) to 2.5 mL of drug solutions with different concentrations and letting the mixture react at room temperature. The proportion of antioxidant activity was determined from the observations made after 30 minutes of observation by measuring the absorbance values at 518 nm. Methanol was applied as the solvent, while ascorbic acid was used as the reference. The estimated percentage of inhibition based on concentration is shown in Figure **4**. The outcomes are shown in Table **6**. Ascorbic acid was the usual medication.

Table 6- Antioxidant activity of new compounds 3(a-l).

Compounds	%Inhibition 20ug	%Inhibition 40ug	%Inhibition 60ug	%Inhibition 80ug	%Inhibition 100ug/ml
3a	22	31	42	53	59
3b	25	31	42	51	58
3c	24	32	43	52	57
3d	22	30	42	53	57
3e	26	32	46	56	58
3f	23	24	22	56	32
3g	21	25	27	54	55
3h	20	22	25	44	50
3i	21	24	27	40	46
3j	22	25	30	37	45
3k	21	26	31	39	44
3l	22	25	33	38	43
	2ug/ml	**4ug/ml**	**6ug/ml**	**8ug/ml**	**10ug/ml**
Ascorbic acid	**10**	**15**	**20**	**33**	**56**

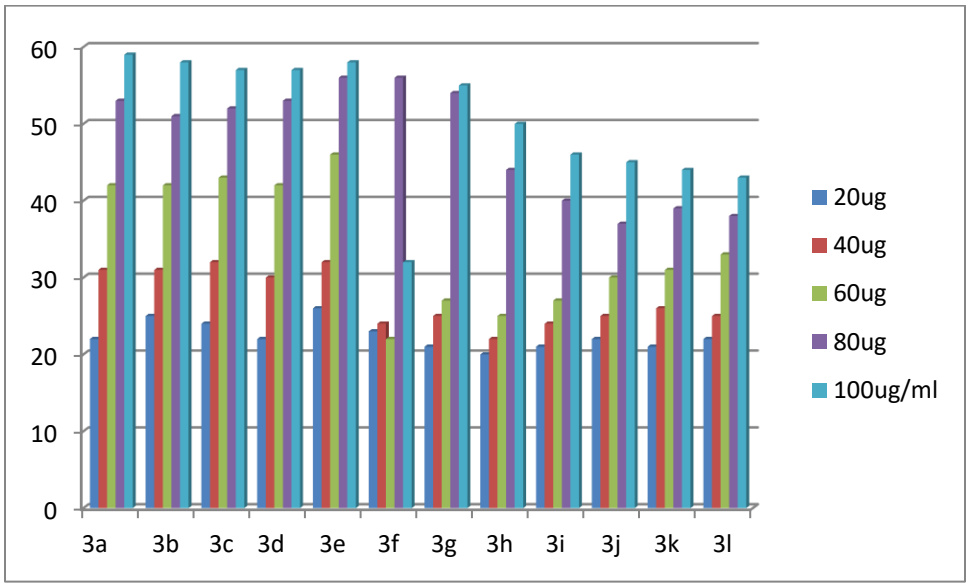


Fig 4- Antioxidant activity of compounds 3(a-l).

5. Result and discursion

The synthetic route for the designed compounds **5 (a-l)** was outlined in Scheme 1. Briefly, the starting material 4-(2-amino-1*H*-imidazol -4-yl) Phenol **(1)** was prepared by stirred for 6 hours

with different aldehydes to give 4-(2-schiffs base-**1*H*-**imidazol -4-yl) Phenol **(2)** was then undergo cyclisation in presence of glacial acetic acid gives 3-[4-(4-hydroxy phenyl)- 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one **3 (a-l).** The compounds **3(a-l)** possessing (hydroxyl phenyl, nitro phenyl, chloral phenyl, methyl phenyl, N (di-methyl phenyl) have shown good antioxidant activity within the series of compounds synthesized. Hence these compounds shall be exploited further for antibacterial activities to attain a potential pharmacophores.

6. Conclusion

In conclusion, we synthesized a series of novel 3-[4-(4-hydroxy phenyl)- 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one **3(a-l)** synthetic method is a simple efficient, inexpensive and easy. These compounds showing good result tested at 100ug/ml concentration against *Escherichia coli*, Pseudomonas *aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris* and fungal cultures such as *Aspergillus niger* and *Candida albicans as compare to simple Thaizolidine*. The compounds 3-[4-(4-hydroxy phenyl)- 1*H*-imidazol -2-yl]-2-phenyl-1, 3-thiazolidin-4-one **3(a-l)** have shown good antioxidant activity.

Declaration of competing interest

The authors affirm that they have no financial stake in the outcome of the work described in the publication.

Data availability

Data will be made available on request.

Supplementary data

Supplementary data to this manuscript can be found online.

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