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DESIGN, SYNTHESIS, CHARACTERIZATION, MOLECULAR DOCKING STUDIES AND ANTHELMINTIC ACTIVITY OF THIOPHENE CONTAIN NOVEL IMIDAZOLE DERIVATIVES

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Abstract

In the present work, we intended to prosper a convenient method for the synthesis of Thiophene contain novel Pyrazole derivatives (3a-3j) by conventional method with Schiff base and halo acetylation mechanism. All the synthesized moieties were proved on the basis spectral analysis. A sequence of novel Imidazole derivatives is screened for Insilco docking studies and anthelmintic activity. In Anthelmintic activity, among this sequence of compounds 3d, 3e, 3h and 3j showed high activity compare with Albendazole as a standard. Molecular docking analysis were performed in order to locate the viable protein ligand like Beta-tubulin interactions of the dataset ligands (3a-3j). Dock rankings of all the synthesized derivatives ranged from -4.07 (compound 3h) to -3.185 (compound 3j). Compound 3h reported highest dock score of -4.070 with Glide binding energy of -37.743 Kcal/mol.

Keywords: Substituted Isatins, 2-methyl imidazole, Thiophene-2-carboxaldehyde, Albendazole, Anthelmintic activity, Molecular Docking.

INTRODUCTION

The nitrogen contains heterocyclic compounds like Imidazole derivatives have a major role in synthetic drugs and biological processes. Medicinal chemistry involves the identification of lead, synthesis and development of new chemical entities suitable for therapeutic use and it also includes the study of existing drugs, their biological properties, and their quantitative structure-activity relationships (QSAR). Isatin and thiophene a class of well- known nitrogen and Sulphur containing heterocyclic admixtures, absorb an important position in medicinal and acaridae chemistry with having a wide range of bioactivities. Imidazole spin-offs have a long history of use in agrochemicals as manures and manures and in pharmaceutical sedulousness as antipyretic andanti-inflammatory [1]. Imidazoles are regarded as a promising class of bioactive heterocyclic compounds that exhibit a wide range of biological activities. Owing to the immense importance and varied by bioactivities exhibited by Imidazole's, efforts have been made from time to time to generate libraries of these compounds and screened them for potential biological activities.

The heterocyclic ring fused imidazole's and its derivations shows remarkable consanguineous and pharmacological exercise as anti - viral exercise, Anthelmintic

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exercise, antibacterial, antifungal, anti-inflammatory, anti-oxidant, antidepressant & anticonvulsant, analgesic, antihistaminic. The Molecular docking studies reveals useful matter about physic receptor intercourses. It analyzes the ribbon frontage of small scrap physic hopefuls to their protein targets in order to prophesy the affinity and exertion of the small scrap. Docking is considered to be a puissant simulation of the molecular recognition process. It's used to illustrate the probable molecular intercourse of a designed ligand with the protein of interest, prophesy the affinity and exertion of the ligand, and identify the energy of the intercourse between the ligand and protein [2-4].

MATERIALS AND METHODS:

General:

In this Investigation all chemicals were purchased from local dealer with S.D fine make was used. The synthesized compounds were screened for anthelmintic, anti-cancer activities. Melting points (MP) were determined in an open capillary and are uncorrected [5-8]. The Fourier-transform infrared spectroscopy (FT-IR) were recorded on Schimadzu FTIR-8400S. The Proton Nuclear magnetic resonance (^{1}H-NMR) spectra were recorded in DMSO-d_6 and chemical shifts (δ) on Bruker DRX-300 MHz. spectrometer using TMS as internal reference with their values expressed in δ ppm[9-12]. Purity of all the synthesized compounds were routinely checked by Thin Layer Chromatography (TLC) on silica gel G in the solvent system (n-Hexane: Ethyl acetate (8:2).

Chemistry:

The acquaint work is finished on Thiophene fused Novel Imidazole derivatives by Conventional method.

Step-I: General procedure for the synthesis of 5-substituted-3-hydrazineylideneindolin-2-one (1a-1e). A mixture of Compound (1a-1e) (0.01mol), hydrazine hydrate (0.01mol), glacial acetic acid (5ml) and Ethanol (30ml) was refluxed for 2-3hr's. The reaction mixture was cooled to room temperature and keep in ice cold water bath to get precipitate. The solid formed dried and crystallization from ethanol.

Step-II: General procedure for the synthesis of 5-substituted-3-((-(substitutedthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one (2a-2j). A mixture of 5-substituted-3-hydrazine ylidene indolin-2-one (1a-1e) (0.01mol), Thiphene-2-carboxaldehyde (0.01mol), glacial acetic acid (5ml) and Ethanol (30ml) was refluxed for 2-3hr's. The reaction mixture was cooled to room temperature and keep in ice cold water bath to get precipitate. The solid formed dried and crystallization from ethanol.

Step-III: General procedure for the synthesis of 2-chloro-1-(1H-imidazol-1-yl) ethan-1-one—dihydrogen. To a solution of 2-methyl imidazole (0.016mol) in (30ml) glacial acetic acid, chloroacetyl chloride (3.7g, 0.032mol) was added drop wise with constant stirring. The reaction mixture was refluxed for 5hrs then it was powered onto

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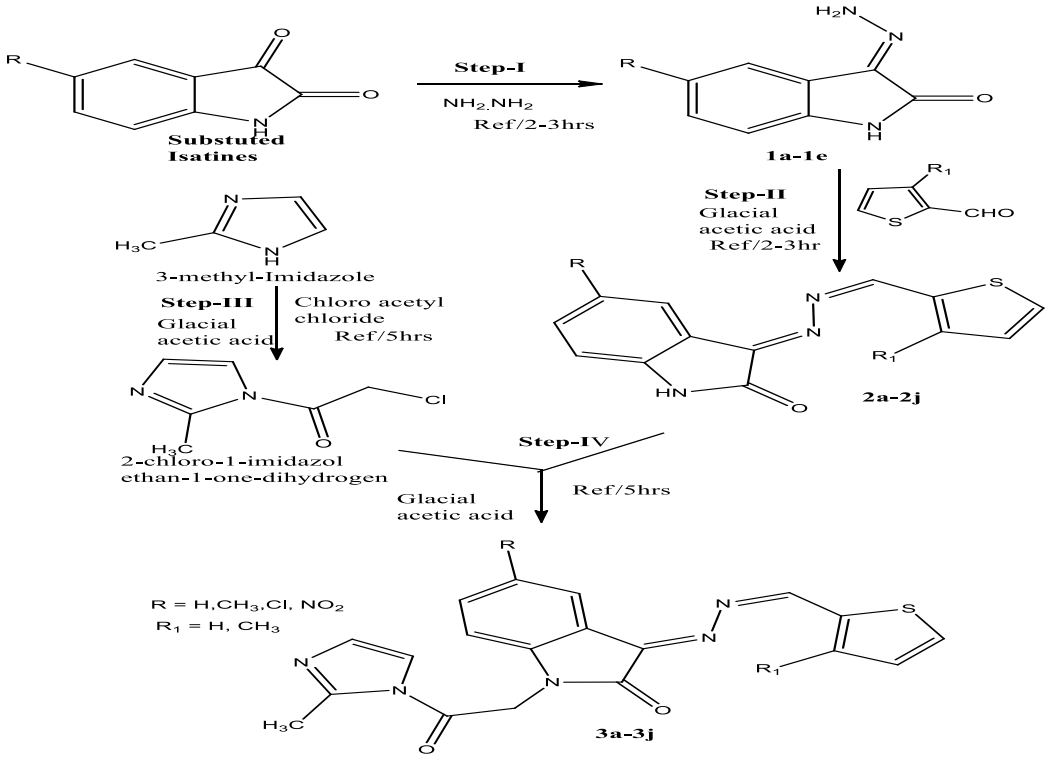
crushed ice. The precipitated solid that obtained was filtered off, washed with cold water, dried and recrystallized from aqueous ethanol.

Step-IV: General procedure for the synthesis of 1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-substituted-3-((-(3-substitutedthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one--dihydrogen (4a-4j). To a solution of 5-substituted-3-(((E)-(3-substitutedthiophen-2-yl)methylene) hydrazine ylidene)indolin-2-one (2a-2j) (0.016mol) in (30ml) glacial acetic acid, 2-chloro-1-(1H-imidazol-1-yl)ethan-1-one--dihydrogen (0.032mol) was added drop wise with constant stirring. The reaction mixture was refluxed for 5 hrs then it was powered onto crushed ice. The precipitated solid that obtained was filtered off, washed with cold water, dried and recrystallized from aqueous ethanol.

Compound.3a. 1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-3-(-(thiophen-2-yl)methylene) hydrazineyli dene)indolin-2-one--dihydrogen: IR, Cm-1 (KBr): 3089(-CH Str, aromatic), 2903, 2827, 2733(-CH Str, aliphatic), 2351(-CSC, Str in Thiaphene), 1707(C=O Str in Indole), 1695(C=O Str in Acetamide), 1616(C=N Str), 1053(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.5995(s, 1H, -CH=N- Imine proton), 7.9770-7.8749(1H, t, Ar-H), 7.8488-7.7833(2H, d, Ar-H), 7.6981-7.6828(2H, d, Ar-H), 7.6060-7.5120(2H, t, Ar-H), 7.4963-7.4806(2H, d, Ar-H), 4.5462(s,2H, -CH_2 protones in acetamide), 1.8343(s, 3H, -CH_3 in Imidazole). Mass (EI-MS): 377(M), 378(M + 1).

Fig No 1: Scheme (Thiophene contain novel Imidazole derivatives)



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Compound.3b:**1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-3-(-(3-methylthiophen-2-yl)methylene) hydrazineylidene)indolin-2-one--dihydrogen** IR, Cm-1 (KBr): 3022(-CH Str, aromatic), 2992, 2842, 2792(-CH Str, aliphatic), 2325(-CSC, Str in Thiaphene), 1713(C=O Str in Indole), 1698(C=O Str in Acetamide), 1591(C=N Str), 1095(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.0031(s, 1H, -CH=N- Imine proton), 8.1035(1H, t, Ar-H), 7.8806-7.8482(2H, d, Ar-H), 7.6810-7.6788(2H, d, Ar-H), 7.6562-7.6335(2H, d, Ar-H), 7.5868-7.5184(1H, t, Ar-H), 4.3945(s,2H, -CH_2 protones in acetamide), 2.0713(s, 3H, -CH_3 in Imidazole), 2.0561(s, 3H, -CH_3 in Theophene). Mass (EI-MS): 391(M), 392(M + 1).

Compound.3c:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methyl-3-(-(thiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3009(-CH Str, aromatic), 2939, 2802, 2764(-CH Str, aliphatic), 2386(-CSC, Str in Thiaphene), 1701(C=O Str in Indole), 1698(C=O Str in Acetamide), 1539(C=N Str), 1046(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.2902(s, 1H, -CH=N- Imine proton), 7.9266-7.8969(2H, d, Ar-H), 7.6856-7.6313(2H, d, Ar-H), 7.5360-7.5202(1H, t, Ar-H), 7.4895-7.3883(2H, t, Ar-H), 6.7295(1H, s, Ar-H), 4.2094-4.2030(s, 2H, -CH_2 protones in acetamide), 1.9847(s, 3H, -CH_3 in Imidazole), 1.8622(s, 3H, -CH_3 in Indole ring). Mass (EI-MS): 391(M), 392(M + 1).

Compound.3d:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-methyl-3-(-(3-methylthiophen-2-yl) meth ylene) hydrazineylidene) indolin-2-one—dihydrogen. 3053(-CH Str, aromatic), 2987, 2843, 2798(-CH Str, aliphatic), 2332(-CSC, Str in Thiaphene), 1712(C=O Str in Indole), 1697(C=O Str in Acetamide), 1567(C=N Str), 1098(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.4632(s, 1H, -CH=N- Imine proton), 8.3721(1H, s, Ar-H), 8.0543-8.0032(2H, d, Ar-H), 7.8743-7.7694(2H, d, Ar-H), 7.4320-7.2027(2H, d, Ar-H), 4.5432-4.4021(s, 2H, -CH_2 protones in acetamide), 2.0532(s, 3H, -CH_3 in Imidazole), 1.9832(s, 3H, -CH_3 in Indole ring), 1.8321(s, 3H, -CH_3 in Theophene). Mass (EI-MS): 405(M), 406(M + 1).

Compound.3e:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-chloro-3-(-(3-methylthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3066(-CH Str, aromatic), 2973, 2865, 2783(-CH Str, aliphatic), 2356(-CSC, Str in Thiaphene), 1721(C=O Str in Indole), 1692(C=O Str in Acetamide), 1587(C=N Str), 1062(C-N, Str), 784(C-Cl, Str in Ar-Cl). ^{1}HNMR (DMSO, δppm): 9.3421(s, 1H, -CH=N- Imine proton), 8.2832(1H, s, Ar-H), 7.9763-7.8069(2H, d, Ar-H), 7.6832-7.4594(2H, d, Ar-H), 7.3980-7.1226(2H, d, Ar-H), 4.3402-4.208(s, 2H, -CH_2 protones in acetamide), 2.2731(s, 3H, -CH_3 in Imidazole), 1.8543(s, 3H, -CH_3 in Theophene). Mass (EI-MS): 425(M), 426(M + 1), 427(M +2).

Compound.3f: 1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-chloro-3-(-(thiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3085(-CH Str, aromatic), 2943, 2829, 2782(-CH Str, aliphatic), 2364(-CSC, Str in Thiaphene), 1719(C=O Str in Indole), 1689(C=O Str in Acetamide), 1548(C=N Str), 1066(C-N, Str), 795(C-Cl, Str in Ar-Cl). ^{1}HNMR (DMSO, δppm): 9.0542(s, 1H, -CH=N- Imine proton), 8.3902(1H, s, Ar-H), 8.2013-8.1023(2H, d, Ar-H), 7.8904-7.6732(2H, d, Ar-H), 7.5421-7.3821(2H, d, Ar-

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H),), 7.2011-7.0132(1H, t, Ar-H), 4.2901-4.1093(s, 2H, -CH_2 protones in acetamide), 2.2012(s, 3H, -CH_3 in Imidazole). Mass (EI-MS): 411(M), 412(M + 1), 413(M +2).

Table No 1: Physical characterization of compounds [3a-3j]

S. Code	R	R_1	Mol. For	Mol.Wt gm/mol	M.P(°C)	%Yield	Rf.V
3a	H	H	$C_{19}H_{15}N_5O_2S$	377.09	168-170	84	0.58
3b	H	-CH_3	$C_{20}H_{17}N_5O_2S$	391.11	125-127	78	0.63
3c	-CH_3	-H	$C_{20}H_{17}N_5O_2S$	391.11	142-144	74	0.79
3d	-CH_3	-CH_3	$C_{21}H_{19}N_5O_2S$	405.13	183-185	70	0.60
3e	-Cl	-CH_3	$C_{20}H_{16}N_5O_2SCl$	425.07	133-136	76	0.59
3f	-Cl	-H	$C_{19}H_{14}N_5O_2SCl$	411.06	154-156	72	0.69
3g	-NO_2	-H	$C_{19}H_{14}N_6O_4S$	422.08	141-143	69	0.72
3h	-NO_2	-CH_3	$C_{20}H_{16}N_6O_4S$	436.10	121-123	68	0.80
3i	-F	-H	$C_{19}H_{14}N_5O_2SF$	395.09	187-189	74	0.76
3j	-F	-CH_3	$C_{20}H_{16}N_5O_2SF$	409.10	129-131	73	0.66

Compound.3g:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-nitro-3-(-(thiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3092(-CH Str, aromatic), 2983, 2882, 2799(-CH Str, aliphatic), 2355(-CSC, Str in Thiaphene), 1721(C=O Str in Indole), 1697(C=O Str in Acetamide), 1634 (C-NO_2, Str in Ar-NO_2), 1593(C=N Str), 1054(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.2902(s, 1H, -CH=N- Imine proton), 8.2984(1H, s, Ar-H), 8.1032-8.0021(2H, d, Ar-H), 7.9542-7.7832(2H, d, Ar-H), 7.6734-7.4521(2H, d, Ar-H), 7.3902-7.2872(1H, t, Ar-H), 4.3291-4.2751(s, 2H, -CH_2 protones in acetamide), 2.0012(s, 3H, -CH_3 in Imidazole). Mass (EI-MS): 422(M), 423(M + 1),

Compound.3h:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-nitro-3-(-(3-methylthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3098(-CH Str, aromatic), 2987, 2845, 2790(-CH Str, aliphatic), 2303(-CSC, Str in Thiaphene), 1711(C=O Str in Indole), 1696(C=O Str in Acetamide), 1624(C-NO_2, Str in Ar-NO_2), 1572(C=N Str), 1098(C-N, Str). ^{1}HNMR (DMSO, δppm): 9.5621(s, 1H, -CH=N- Imine proton), 8.3421(1H, s, Ar-H), 8.1032-8.0012(2H, d, Ar-H), 7.8322-7.7632(2H, d, Ar-H), 7.5432-7.3621(2H, d, Ar-H), 4.2891-4.1092(s, 2H, -CH_2 protones in acetamide), 2.1092(s, 3H, -CH_3 in Imidazole). 1.9902(s, 3H, -CH_3 in Theophene). Mass (EI-MS): 436(M), 437(M + 1), 427(M +2).

Compound.3i:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-fluoro-3-(-(thiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3067(-CH Str, aromatic), 2941, 2878, 2786(-CH Str, aliphatic), 2301(-CSC, Str in Thiaphene), 1703(C=O Str in Indole), 1685(C=O Str in Acetamide), 1578(C=N Str), 1092(C-N, Str), 802(C-F, Str in Ar-F). ^{1}HNMR (DMSO, δppm): 9.2903(s, 1H, -CH=N- Imine proton), 8.2092(1H, s, Ar-H), 7.9032-7.8932(2H, d, Ar-H), 7.6212-7.4892(2H, d, Ar-H), 7.2903-7.1022(2H, d, Ar-H), 6.9821-6.8932(1H, t, Ar-H), 4.1092-4.0983(s, 2H, -CH_2 protones in acetamide), 2.1023(s, 3H, -CH_3 in Imidazole). Mass (EI-MS): 395(M), 396(M + 1), 397(M +2).

Compound.3j:1-(2-(1H-imidazol-1-yl)-2-oxoethyl)-5-fluoro-3-(-(3-methylthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one—dihydrogen. 3029(-CH Str, aromatic), 2956, 2878, 2723(-CH Str, aliphatic), 2303(-CSC, Str in Thiaphene),

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1719(C=O Str in Indole), 1689(C=O Str in Acetamide), 1573(C=N Str), 1099(C-N, Str), 834(C-F, Str in Ar-F). ^{1}HNMR (DMSO, δppm): 9.6732(s, 1H, -CH=N- Imine proton), 8.4821(1H, s, Ar-H), 8.0213-8.0023(2H, d, Ar-H), 7.7832-7.6521(2H, d, Ar-H), 7.1750-7.0532(2H, d, Ar-H), 4.2987-4.2002(s, 2H, -CH_2 protones in acetamide), 2.1908(s, 3H, -CH_3 in Imidazole), 1.9832(s, 3H, -CH_3 in Theophene). Mass (EI-MS): 409(M), 410(M + 1), 411(M +2).

Pharmacological activity:

Anthelmintic activity: The synthesized novel thiophene fused Imidazole derivatives are tested for anthelminthic activity by using the Indian Earth worms. Almost equal measurement of six earthworms had been positioned in preferred drug solution and take a look at compound's options at room temperature. Normal saline used as control [16-17]. The widespread drug and check compounds have been dissolved in minimal volume of dimethyl sulfoxide (DMSO) and adjusted the extent up to 10 ml with regular saline answer to get the attention of 0.1% w/v, 0.2 percent w/v and 0.5% w/v. Albendazole was once used as a widespread drug. The compounds had been evaluated by way of the time taken for whole paralysis and loss of life of earthworms (Figure-3). The imply deadly time for every check compound used to be recorded and in contrast with trendy drug. The time taken via worms to turn out to be immobile was once cited as paralysis time. To verify the dying of the immobile worms had been regularly utilized with exterior stimuli, which stimulate and set off motion in the worms, if alive. The suggest deadly time and paralysis time of the earthworms for specific check compounds and general drug are tabulated in Table No.2.

Table No 2: Anthelmintic activity of thiophene contain novel Imidazole derivatives (3a-3j)

S.No.	Compound	Time in minutes					
		For paralysis % Concentration			For death % Concentration		
	Concentration	0.1	0.2	0.5	0.1	0.2	0.5
	Control	-	-	-	-	-	-
	Albendazole	20	14	9	40	32	25
1	3a	30	28	21	53	46	38
2	3b	31	29	20	56	49	35
3	3c	28	21	19	50	43	34
4	3d	**25**	**21**	**17**	**45**	**39**	**30**
5	3e	**24**	**20**	**16**	**46**	**40**	**32**
6	3f	34	23	19	51	47	32
7	3g	37	32	23	59	48	34
8	3h	**24**	**17**	**15**	**46**	**38**	**30**
9	3i	33	27	23	61	54	38
10	3j	**23**	**18**	**13**	**44**	**35**	**29**

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Figure No 3: Graphical representation of anthelmintic activity of thiophene contain novel Imidazole derivatives (3a-3j) – Paralysis time (min)

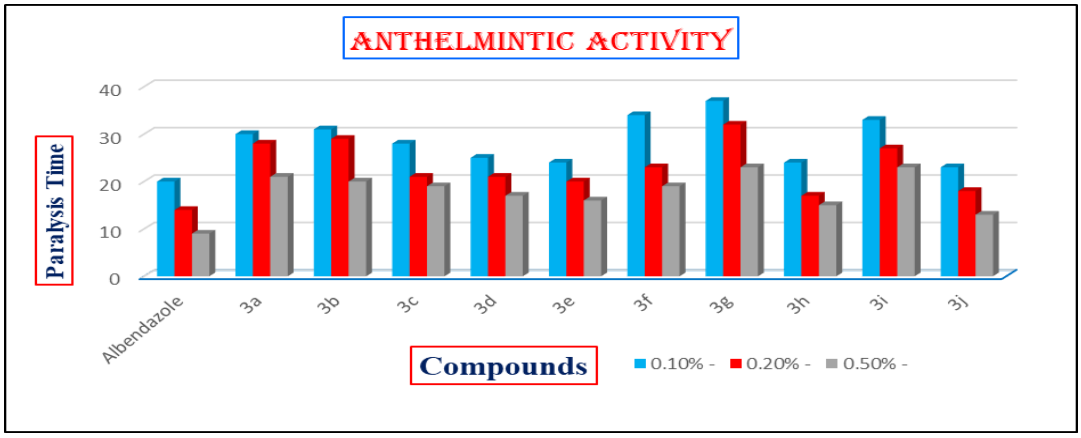


Figure No 4: Graphical representation of anthelmintic activity of Thiophene contain novel Imidazole derivatives (3a-3j) – Death time (min)

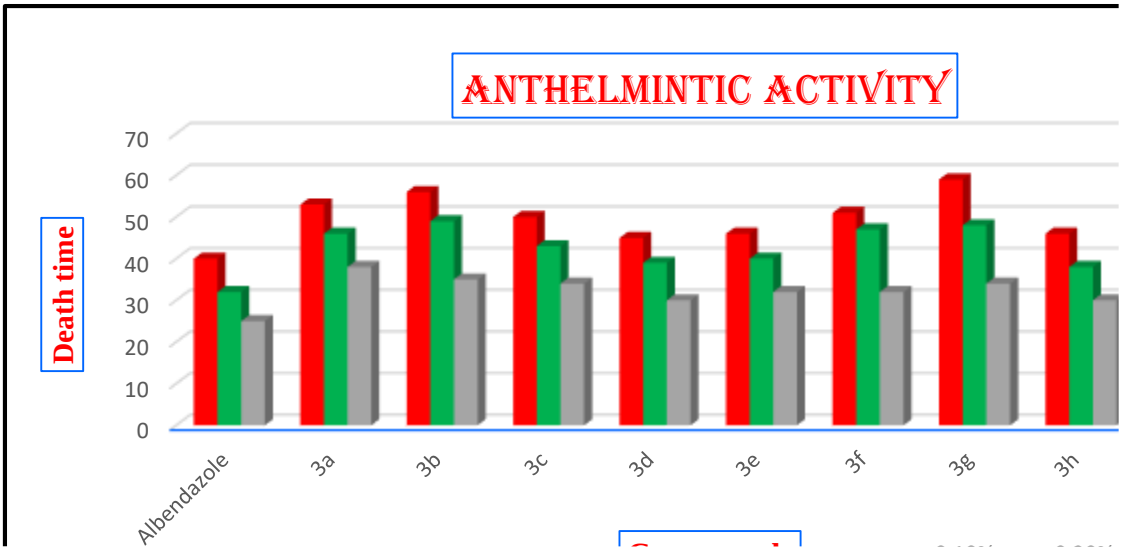
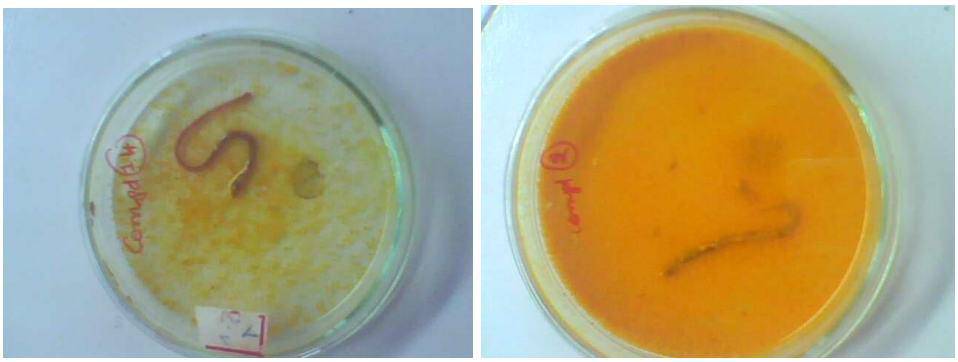


Figure 3: Photograph for copound-3b and 3d-Anthelmintic activity



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Molecular Docking Studies: The digital structure of the Acetylcholine-binding protein (AChBP) used to be retrieved from the Protein databank website with PDB Id: 2ZJU and the structure was once optimized via deleting unbound water molecules which are over 1 Å, adding hydrogen atoms to satisfy the valences, adding lacking amino acids to stabilize aspect chains and power of the whole structure was minimized using OPLS-2005 force discipline the usage of Protein Preparation Wizard tool of Schrodinger Suite. Thus structurally optimized protein shape was used to have a look at protein ligand interactions of the dataset ligands the use of Glide Xp docking protocol. Initially, a 3D grid was hooked up to the binding pocket (active site) of the protein, into which all the dataset ligands have been docked into. Binding interactions and efficiency of the binding were calculated in phrases of Glide Score, which is a mixture of hydrophilic, hydrophobic, metal binding groups, Van der Waals energy, freezing rotatable bonds and polar interactions with receptor. GScore = 0.065 x Van der Waals energy + 0.130 x Coulomb energy + Lipophilic term (Hydrophobic interactions) + H bonding + Metal binding + BuryP (Penalty for buried polar groups) + RotB (Penalty for freezing rotatable bonds) + Site (Polar interactions in the active site).

Table No 3: Insilico EGFR inhibition of Thiophene contain novel Imidazole derivatives -Glide dock sores of the dataset ligands

Compound No	Dock score XP GScore	No of H-bonds	Interacting amino acids	H-bond lengths (Å)	Emodel energy	Glide energy
3h	-4.07	1	LYS 721	1.89	-46.182	-37.743
3d	-3.974	1	CYS 773	2.04	-46.706	-38.635
3e	-3.272	0	-	-	-43.988	-36.898
3j	-3.185	0	Met 769	2.13	-39.868	-32.656
3c	-2.432	1	LYS 721 MET 769	1.60 1.13	-31.484	-31.663
3b	-2.326	0	CYS 773	1.90	-30.464	-39.552
3f	-2.29	1	LYS 721	1.89	-32.083	-30.721

RESULTS AND DISCUSSION:

Thiophene contain novel Imidazole derivatives (3a-3j) was performed in 4 steps (fig.1). The acquaint work is finished on substituted isatins with hydrazine hydrate to give 5-substituted-3-hydrazineylideneindolin-2-one (1a-1e). Then it was go through Schiff's base mechanism with thiophene-2-carboxaldehyde to produce 5-substituted-3-((-(substitutedthiophen-2-yl) methylene) hydrazineylidene) indolin-2-one (2a-2j [13]. In 3rd step, 2-methyl imidazole reacts with chloroacetyl chloride to form 2-chloro-1-(1H-imidazol-1-yl) ethan-1-one-dihydrogen, it was reacting with compound (2a-2j) in final step in the presence of glacial acetic acid to give the title products (3a-3j). The reaction was observed by TLC (Hexane: EtoAc 8:2) method. The solid was filtered off and washed with hexane solvent and recrystallized from ethanol to get a crystalline product. The obtained compounds were subjected to analytical by physical characterization (Table.No-1). The synthesized thiophene contain novel Imidazole derivatives were screened for them in vitro anthelmintic activity, and Molecular Docking

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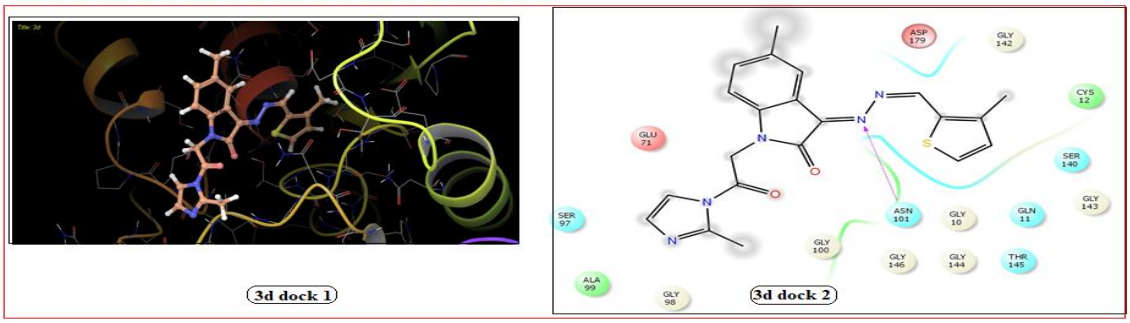
studies. All the compounds are characterized by Physical and Spectral data, which were confirmed on by using IR, ^{1}H NMR and LC-MS data.

The Thiophene contain novel Imidazole derivatives (3a-3j) was characterized by primarily IR spectroscopy. Practically, all of the compounds have the C-H stretching frequency in aromatic and aliphatic, as expected is observed at around 3000-3090 cm^{-1} and at 2990-2720 $cm^{-1.}$ Correspondently. All the compounds containing the strong absorption peak observed at around at 2300-2390 cm^{-1} and 1680-1730 cm^{-1} is found to be presence of C-S-C and C=O stretching frequency in Thiophene and Indole, Acetamide group. In all of the compounds has showing C=N stretching around at 1600-1640cm^{-1} respectively. The C=C stretching is attributed to the strong absorption in the region 1505-1554 cm^{-1}. The compounds containing -CH_3 group shows peaks due to asymmetric and symmetric bending of –OCH_3 group is observed at around 1256 cm^{-1} and 1043 cm^{-1} and C-Cl stretching is attributed to the strong absorption in the region 782-835 cm^{-1}. Similarly, the ^{1}HNMR (DMSO-d6) spectra of thiophene fused novel Imidazole derivatives showing a singlet at δ 9.002-9.685 for -CH=N- Imine proton. All the synthesized compounds showing a triplet and singlet at around δ 6.794-8.483 for aromatic CH protons. All the compound has Acetamide protons were found doublet of singlet protons (-CH_2-CO-) around at δ 4.402-4.893 ppm. And δ 1.801-2.032 was absolved in some derivatives are showing the –CH_3 protons in Imidazole.

All the newly synthesized compounds (3a-3j) were evaluated for anthelmintic activity on Indian earthworms (Pheretima posthuma) as shown in table.2. Among, all the compounds were showed significant paralytic and death time of earthworms by compared to standard drug such as albendazole. All the test and standard drugs are prepared at 0.1%, 0.2% and 0.5% concentrations. A closer inspiration of data from this table indicated that compound **3d, 3e, 3h** and **3j** having more activity. For Molecular Docking studies of all the synthesized derivatives ranged from -4.07 (compound 3h) to -3.185 (compound 3j). Compound 3h reported highest dock score of -4.070 with Glide binding energy of -37.743 Kcal/mol.

Figure 5: Docking Pose between the Ligand and the Protein (Dock1 and Dock-2)



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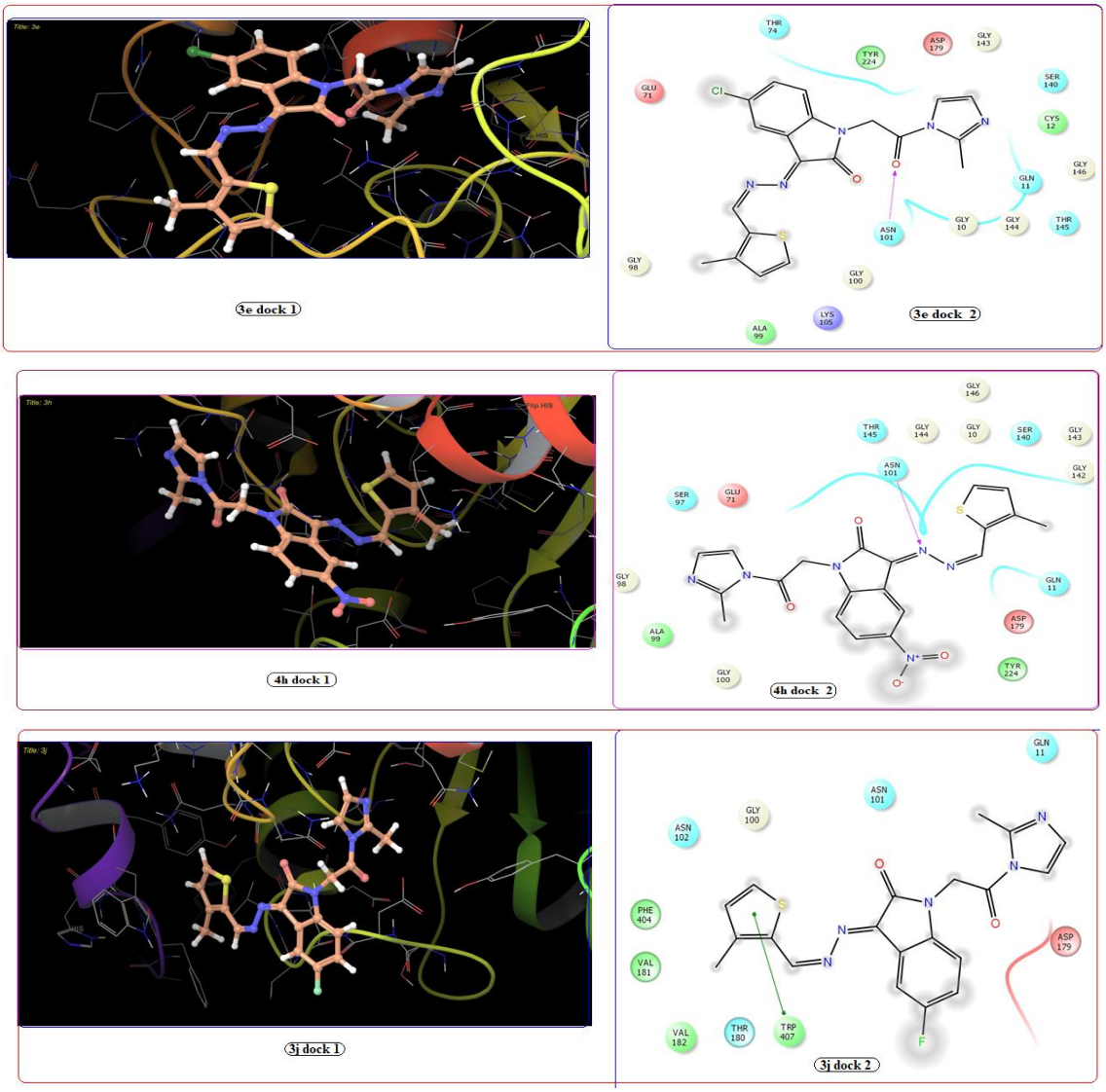

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