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Research article

Design, synthesis and biological screening of novel heterocyclic ring derivatives as antibacterial agents

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ABSTRACT

For a long time, numerous attempts are being made by researchers to discover and develop new antimicrobial agents based on synthetic compounds and medicinal plants. These attempts were forced due to increasing rate of microbial resistance. In the present study, it has been discussed that the synthesis of various dihydropyrimidine fused with benzimidazole moiety. In which o-phenylenediamine and chloroacetic acid react in acidic medium by nucleophilic addition reaction to form 2-chloro methyl Benzimidazole. (1). The substituted Chalcone (2) was synthesized by a claisan-schmidt condensation reaction. The condensation of an aromatic aldehyde with aromatic ketone having α- hydrogen in presence of a strong base to form α,β-unsaturated ketone i.e Chalcone is form. The substituted Chalcone react with thiourea by Michael reaction. It is also called 1,4 addition reaction. In which thiourea act as nucleophile attack on 4-positon of the α,β-unsaturated ketone and keto-enol tautomerism occurs and 4-substitutedphenyl-6-substitutedphenyl-4,5-dihydropyrimidine-2- thiol . (3). Benzimidazole (1) fused with substituted dihydropyrimidine-2-thiol (3) in presence of THF and form 2-((4-substituted phenyl-6-substituted phenyl pyrimidine-2-ylthio)methyl)-1*H*-benzo[d]imidazole. (4). The synthesized compounds APUS1 – APUS21 were assigned by its spectral data (IR, NMR and mass spectra). The synthesized compounds have been tested for their antibacterial activity against Gram (+) bacteria (*S. aureus*) , (*B.subtilis*) and Gram (-) bacteria (*E.coli*) by agar diffusion method. Compound having electron withdrawing group show significant activity and having electron donor group show moderate activity.

Keywords: Antibacterial activity, Molecular docking, Dihydropyrimidine, Benzimidazole.

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INTRODUCTION

Day by day there has been increasing consumption of various antibiotics for the treatment of microbial infections which leads to emergence of multi-drug resistant microbial pathogens. Therefore, there is an urgent demand for research and synthesis of novel of antimicrobial agents having different mode of action which should be effective against various types of bacteria and fungi to solve the problem of microbial resistance.

Heterocyclic compounds containing nitrogen are promising structure moiety for drug design. Benzimidazole and Pyrimidines, Dihydropyrimidines are one of the important heterocyclic compounds, show a diverse range of biological activities such as, antibacterial, antimicrobial, antifungal, antitubercular, anti-inflammatory, anticancer.

Benzimidazole nucleus is the key building block for a variety of compounds that play crucial roles in the function of a number of biologically important molecules. The recent identification of a DHPM analog as a potential new antibacterial lead.

Hence, many synthetic methodologies have been established to synthesis many benzimidazole and DHPM derivatives. On present work chalcone was react with thiourea to form substituted dihydrophrimidine. It was conjugated with benzimidazole with Sulphur atom.

Accordingly, the focus of the present work is the synthesis and characterization of some new benzimidazole-pyrimidine conjugate moieties. All targets have been checked as antibacterial agents using agar diffusion method against gram-positive bacteria (Staphylococcus aureus and B. subtilis), gram-negative bacteria (Escherichia coli). The possible mode of action was tested using molecular docking study.

Molecular docking is a theoretical approach aiming to accurately predict the binding of macro molecules and a small ligand. In this aspect, we employed docking analysis to predict the docking

models of the tested compounds in the binding pocket of bacterial proteins (DNA gyrase subunit B) that are known targets for some antibiotics. [1-16]

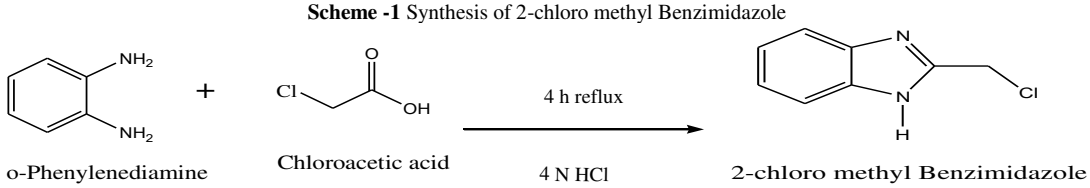
MATERIALS AND METHODS

Melting points of the synthesized compounds were determined in open capillary tubes and were uncorrected. Reaction Progress was observed by TLC plates. IR spectra were recorded on FT/IR-400 spectro-photometer using KBr disc method. The 1H-NMR spectra were recorded on sophisticated multinuclear FT-NMR Spectrometer model (Bruker), using dimethylsulfoxide-d6 as solvent.

Synthesis of 2-chloro methyl Benzimidazole: [17]

In a 250 ml round bottom flask, o-Phenylenediamine (10.8 g.), chloroacetic acid (14.2 g.) and 4N hydrochloric acid (100 cc.) were heated under reflux for 4 hrs. The mixture was allowed to stand overnight, filtered, diluted with 200 cc. of water, cooled and carefully neutralized with 6N ammonium hydroxide solution. The solution kept in cold condition during the neutralization and stirred vigorously. The product was filtered, washed well with cold water, and dried. It was recrystallised from methanol-water mixture.

Scheme -1 Synthesis of 2-chloro methyl Benzimidazole



o-Phenylenediamine Chloroacetic acid 2-chloro methyl Benzimidazole

Table 2.1: Physical properties of 2-chloro methyl Benzimidazole:

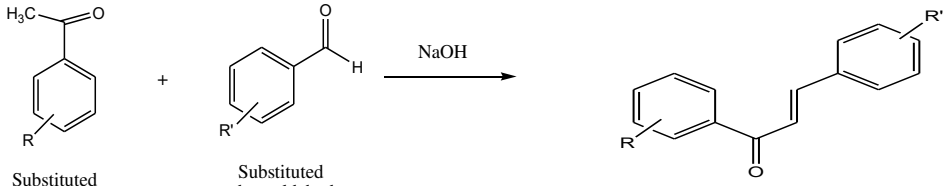
Molecular formula	$C_8H_7ClN_2$
Mol. Wt.	166.61
% Yield	80-85%
Melting point	145-147°C
R_f value*	0.75

* Solvent system- Benzene: methanol (9:1)

Synthesis of substituted Chalcone (Benzylidinacetophenone)[18]

A solution of sodium hydroxide (2.2 g) in water (20 ml) and rectified spirit (15 ml) was taken in a conical flask and cooled in an ice bath. To the cooled solution, acetophenone (5 ml) was added followed by the addition of benzaldehyde (4.4 ml). The reaction mixture was stirred and the temperature of the reaction mixture kept at about 25°C. The mixture was stirred till the mixture becomes viscous and no more stirring was effective. The mixture was kept overnight in a refrigerator. The separated product was filtered and washed well with cold water. It was recrystallised from rectified spirit.

Scheme -2 Synthesis of substituted Chalcone (Benzylidinacetophenone)



Substituted Acetophenone Substituted benzaldehyde Substituted Chalcone

Table 1: Physical properties of substituted chalcone:

Code No.	R	R'	Mol. Formula	Mol. Wt.	% yield	M.P (ºC)	*R_f value
APUS1	H	H	$C_{15}H_{12}O$	208.26	85	55-56	0.35
APUS2	H	4-Cl	$C_{15}H_{11}ClO$	242.7	91	87-89	0.45
APUS3	H	2-Cl	$C_{15}H_{11}ClO$	242.7	87	47-48	0.38
APUS4	H	4-NO2	$C_{15}H_{11}NO_3$	253.25	65	124-126	0.55
APUS5	H	2-NO2	$C_{15}H_{11}NO_3$	253.25	72	94-96	0.62
APUS6	H	3-NO2	$C_{15}H_{11}NO_3$	253.25	70	38-40	0.40
APUS7	H	4-OH	$C_{15}H_{12}O_2$	224.25	72	135-138	0.48
APUS8	H	2-OH	$C_{15}H_{12}O_2$	224.25	65	125-127	0.75
APUS9	H	4-CH3	$C_{16}H_{14}O$	222.29	82	80-82	0.88
APUS10	4-Cl	H	$C_{15}H_{11}ClO$	242.7	75	68-70	0.69
APUS11	4-OCH3	H	$C_{16}H_{14}O2$	238.28	72	75-77	0.64
APUS12	3-NO2	H	$C_{15}H_{11}NO_3$	253.25	82	80-82	0.58
APUS13	4-NH2	H	$C_{15}H_{13}NO$	223.27	73	70-72	0.81
APUS14	3-NH2	H	$C_{15}H_{13}NO$	223.27	76	74-76	0.76
APUS15	4-F	H	$C_{15}H_{11}FO$	226.26	82	82-84	0.49
APUS16	3-Br	H	$C_{15}H_{11}BrO$	287.15	78	72-74	0.55
APUS17	4-Br	H	$C_{15}H_{11}BrO$	287.15	75	74-77	0.80
APUS18	4-OCH3	4-Cl	$C_{16}H_{13}ClO_2$	272.73	85	76-79	0.61
APUS19	4-Br	3-NO2	$C_{15}H_{10}BrNO_3$	332.15	78	80-82	0.52
APUS20	3-NO2	4-OH	$C_{15}H_{11}NO_4$	269.25	82	125-127	0.47
APUS21	4-F	4-CH3	$C_{16}H_{13}FO$	240.27	85	112-114	0.51

* Solvent system- Benzene: methanol (9:1)

Synthesis of 4-substitutedphenyl-6-substitutedphenyl-4,5-dihydropyrimidine-2-thiol

The synthesized Chalcone(7g), thiourea (2.1g), ethanol(40ml) and K_2CO_3 was taken in to a flask. The flask put in to the reflux assembly and refluxed for 7 hrs. The reaction mixture was allowed to stand

overnight, filtered and collect the product. It was recrystllized from ethanol.

Scheme -3 Synthesis of 4-substitutedphenyl-6-substitutedphenyl-4,5-dihydropyrimidine-2-thiol derivatives

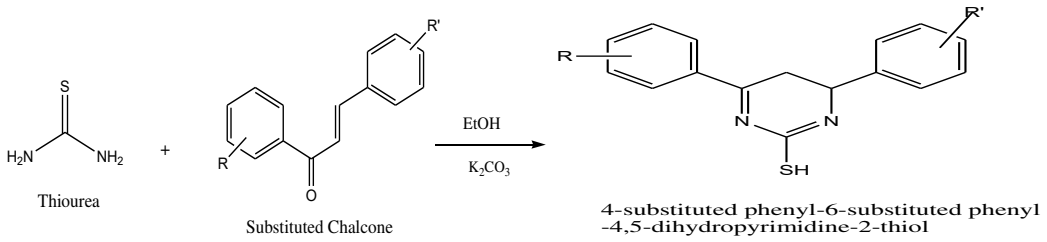


Table 2: Physical properties of 4-substitutedphenyl-6-substitutedphenyl-4,5- dihydropyrimidine-2-thiol

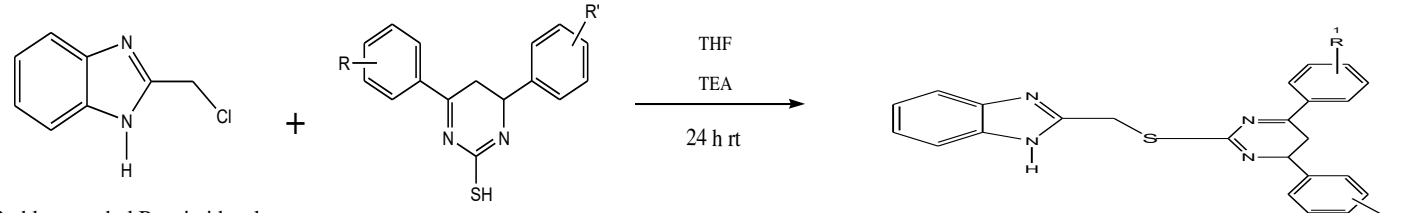
Code No.	R	R'	Mol. Formula	Mol. Wt.	% yield	M.P (ºC)	*R_f value
APUS1	H	H	$C_{16}H_{14}N_2S$	266.36	65	153-155	0.65
APUS2	H	4-Cl	$C_{16}H_{13}ClN_2S$	300.81	70	66-68	0.58
APUS3	H	2-Cl	$C_{16}H_{13}ClN_2S$	300.81	67	177-180	0.71
APUS4	H	4-NO2	$C_{16}H_{13}N_3O_2S$	311.36	55	60-62	0.68
APUS5	H	2-NO2	$C_{16}H_{13}N_3O_2S$	311.36	62	50-52	0.80
APUS6	H	3-NO2	$C_{16}H_{13}N_3O_2S$	311.36	63	53-55	0.85
APUS7	H	4-OH	$C_{16}H_{14}N_2OS$	282.36	62	80-82	0.76
APUS8	H	2-OH	$C_{16}H_{14}N_2OS$	282.36	55	67-70	0.57
APUS9	H	4-CH3	$C_{17}H_{16}N_2S$	280.39	66	94-96	0.45
APUS10	4-Cl	H	$C_{16}H_{13}ClN_2S$	300.81	65	67-71	0.38
APUS11	4-OCH3	H	$C_{17}H_{16}N_2OS$	296.39	62	92-94	0.72
APUS12	3-NO2	H	$C_{16}H_{13}N_3O_2S$	311.36	71	92-94	0.66
APUS13	4-NH2	H	$C_{16}H_{15}N_3S$	281.38	67	84-87	0.55
APUS14	3-NH2	H	$C_{16}H_{15}N_3S$	281.38	62	80-82	0.64
APUS15	4-F	H	$C_{16}H_{13}FN_2S$	284.35	68	94-96	0.50
APUS16	3-Br	H	$C_{16}H_{13}BrN_2S$	345.26	64	168-170	0.49
APUS17	4-Br	H	$C_{16}H_{13}BrN_2S$	345.26	65	175-177	0.53
APUS18	4-OCH3	4-Cl	$C_{17}H_{15}ClN_2OS$	330.83	71	98-101	0.58
APUS19	4-Br	3-NO2	$C_{16}H_{12}BrN_3O_2S$	390.25	62	94-96	0.61
APUS20	3-NO2	4-OH	$C_{16}H_{13}N_3O_3S$	327.36	70	76-77	0.78
APUS21	4-F	4-CH3	$C_{17}H_{15}FN_2S$	298.37	72	82-84	0.62

*Solvent system- Benzene:methanol (9:1)

Table 3: Physical properties of substituted dihydropyrimidine-benzimidazole derivatives

Code No.	R	R'	Mol. Formula	Mol. Wt.	% yield	M.P (ºC)	*R_f value
APUS1	H	H	$C_{24}H_{20}N_4S$	396.51	60	95-98	0.38
APUS2	H	4-Cl	$C_{24}H_{19}ClN_4S$	430.95	65	78-80	0.45
APUS3	H	2-Cl	$C_{24}H_{19}ClN_4S$	430.95	62	74-76	0.72
APUS4	H	4-NO_2	$C_{24}H_{19}N_5O_2S$	441.5	52	112-114	0.66
APUS5	H	2-NO_2	$C_{24}H_{19}N_5O_2S$	441.5	58	75-78	0.81
APUS6	H	3-NO_2	$C_{24}H_{19}N_5O_2S$	441.5	63	78-80	0.83
APUS7	H	4-OH	$C_{24}H_{20}N_4OS$	412.51	61	92-94	0.76
APUS8	H	2-OH	$C_{24}H_{20}N_4OS$	412.51	58	84-86	0.54
APUS9	H	4-CH_3	$C_{25}H_{22}N_4S$	410.53	63	55-58	0.45
APUS10	4-Cl	H	$C_{24}H_{19}ClN_4S$	430.95	65	52-54	0.38
APUS11	4-OCH_3	H	$C_{25}H_{22}N_4OS$	426.53	62	45-47	0.70
APUS12	3-NO_2	H	$C_{24}H_{19}N_5O_2S$	441.5	71	56-58	0.61
APUS13	4-NH_2	H	$C_{24}H_{21}N_5S$	411.52	65	80-82	0.57
APUS14	3-NH_2	H	$C_{24}H_{21}N_5S$	411.52	60	55-57	0.62
APUS15	4-F	H	$C_{24}H_{19}FN_4S$	414.5	62	52-54	0.55
APUS16	3-Br	H	$C_{24}H_{19}BrN_4S$	475.4	58	40-42	0.45
APUS17	4-Br	H	$C_{24}H_{19}BrN_4S$	475.4	65	71-73	0.53
APUS18	4-OCH_3	4-Cl	$C_{25}H_{21}ClN_4OS$	460.98	72	74-75	0.48
APUS19	4-Br	3-NO_2	$C_{24}H_{18}BrN_5O_2S$	520.4	62	80-81	0.65
APUS20	3-NO_2	4-OH	$C_{24}H_{19}N_5O_3S$	457.5	68	68-70	0.78
APUS21	4-F	4-CH_3	$C_{25}H_{21}FN_4S$	428.52	72	94-96	0.52

Scheme -4 Synthesis of substituted dihydropyrimidine Benzimidazole derivatives



2-chloro methyl Benzimidazole

4-substituted phenyl-6-substituted phenyl -4,5-dihydropyrimidine-2-thiol

2-((4,6- diphenyl-4,5-dihydropyrimidin-2-ylthio)methyl)-1H-benzoimidazole

1 **3** **4**

Synthesis of substituted dihydropyrimidine Benzimidazole derivatives:

General procedure for APUS1 –APUS21

A solution of the 4,6-diphenyl-4,5-dihydropyrimidine-2-thiol derivatives (42.17 mmol) in dry tetrahydrofuran (60 ml) and triethylamine (0.5 ml) was stirred for 1 h. A solution of 2-chloro methyl benzimidazole (42.17 mmol) in dry tetrahydrofuran was then added portion wise and the reaction mixture was stirred at room temperature for additional 24 h, poured into crushed ice with stirring. The precipitated product was filtered off. It was recrystalized from methanol.

Spectroscopic characterization

Table 4: Spectral data of synthesized dihydropyrimidine derivatives

Compound code	Mol.wt	Mass m/e	^{1}H NMR(δ ppm)	IR(cm^{-1})
APUS1	396.51	397 (M+1)	8.3-7.1 (m,14H, Ar-H)	3480 N-H streatching
			5.6 (s,1H, N-H)	3147-3016 Ar. C-H
			5.2-4.8 (s, 2H, CH_2-S)	2818 Ali. C-H
			4.5-4.4 (m, 2H, CH_2)	1228 C-N ,
			3.3 (s,1H, C-H)	1625 C=N
APUS2	430.95		7.9-7.1 (m,13H, Ar-H),	3082-3005 Ar C-H
			3.3 (s,1H, N-H),	2951-2897 Ali. C-H
			3.4-3.3 (s, 2H, CH_2-S),	1278 C-N ,
			3.49-3.41 (d, 2H, CH_2),	1681 C=N
			3.8 (m,1H, C-H).	752 C-Cl
APUS3	430.95		----	3367 N-H streatching
				3136-3022 Ar. C-H
				2991-2941 Ali. C-H
				1271 C-N , 1620 C=N
				742 C-Cl
APUS4	441.5	440.13 (M-1)	----	3103-3059 Ar. C-H
				2916-2848 Ali. C-H
				1517,1344 N=O
				1595 N-H bending
APUS5	441.5		7.5-6.4 (m,13H, Ar-H),	3387 N-H streatching
			4.6 (s,1H, N-H),	3057-3010 Ar. C-H
			5.06(s, 2H, CH_2-S),	2978-2891 Ali. C-H
			4.6 (d, 2H, CH_2),	1274 C-N
			4.5 (s,1H, C-H).	1658 C=N
				1546,1336 N=O
				1602 N-H bending
APUS6	441.5			3338 N-H streatching
				3059 Ar C-H
				2972-2868 Ali. C-H
				1271 C-N
				1683 C=N
				1527,1348 N=O
				1595 N-H bending
APUS7	412.51			3504 O-H streatching
				3053-3003 Ar. C-H
				2953-2881 Ali. C-H
				1273 C-N
				1618 C=N
				1598 N-H bending
APUS8	412.51			3601 O-H streatching
				3169-3008 Ar. C-H
				2997-2846 Ali. C-H
				1273 C-N
				1597 N-H bending
APUS9	410.53	409.18 (M-1)		3321 N-H streatching
				3055-3005 Ar. C-H
				2978-2891 Ali. C-H
				1273 C-N
				1681 C=N
				1597 N-H bending
APUS10	430.95	431.09 (M+1)		3170-3028 Ar. C-H
				2900 Ali. C-H
				1271 C-N ,
				1681 C=N
				1587 N-H bending
				761 C-Cl
APUS11	426.53	425.15 (M-1)	8.1-7.1 (m,13H, Ar-H),	3057 Ar C-H
			2.5 (s,1H, N-H),	2933-2837 Ali. C-H
			3.88 (s, 2H, CH_2-S),	1259 C-N ,
			3.83 (O-CH_3),	1658 C=N
			3.3-2.5 (m, 2H, CH_2),	1598 N-H bending
			2.5 (s,1H, C-H).	1170 C-O

APUS12	441.15	440.13 (M-1)	8.0-7.1 (m,13H, Ar-H),	3365 N-H streatching
			2.51 (s,1H, N-H),	3167-3059 Ar. C-H
			4.8 (s, 2H, CH_2-S),	2866 Ali. C-H
			3.6 (d, 2H, CH_2),	1666 C=N
			1.8 (s,1H, C-H).	1529,1348 N=O
				1600 N-H bending
APUS13	411.52		7.9-7.0 (m,13H, Ar-H),	3558,3537,3518 N-H streatching
			3.3 (s,1H, N-H),	
			4.5 (NH_2),	3130-3026 Ar. C-H
			4.3 (s, 2H, CH_2-S),	2949-2845 Ali. C-H
			3.6 (d, 2H, CH_2),	1273 C-N
			1.8 (s,1H, C-H)	1645 C=N
				1595 N-H bending
APUS14	411.52	410.18 (M-1)		3448,3367,3213 N-H streatching
				3078-3026 Aro. C-H
				2974-2902 Ali. C-H
				1186 C-N
				1674 C=N
				1598, 1579 N-H bending
APUS15	414.5		8.3-7.1 (m,13H, Ar-H),	3061-3026 Ar. C-H
			3.8 (s,1H, N-H),	2916-2848 Ali. C-H
			5.6-5.5 (s, 2H, CH_2-S),	1157 C-N
			3.4 (d, 2H, CH_2),	1681 C=N
			3.5 (s,1H, C-H).	1597 N-H bending
				1205 C-F
APUS16	475.4		8.2-7.0 (m,13H, Ar-H),	3313 N-H streatching
			3.8 (s, 2H, CH_2-S),	3061-3028 Ar. C-H
			3.4 (d, 2H, CH_2),	2980-2902 Ali. C-H
			2.9 (s,1H, C-H).	1685 C=N
				1597 N-H bending
				700 C-Br
APUS17	475.4			3356 N-H streatching
				3078-3001 Ar. C-H
				2976-2897 Ali. C-H
				1273 C-N
				1647 C=N
				1595 N-H bending
				700 B-Br
APUS18	460.98	461.14 (M+1)	8.1-7.0 (m,12H, Ar-H),	3307 N-H streatching
			3.88 (s,1H, N-H),	3169-3012 Ar. C-H
			3.88 (s, 3H, O-CH_3)	2962-2839 Ali. C-H
			3.84 (s, 2H, CH_2-S),	1255 C-N ,1656 C=N
			3.33 (d, 2H, CH_2),	1604 N-H bending
			2.4 (s,1H, C-H).	1111 C-O , 746 C-Cl
APUS19	420.4			3147-3064 Ar. C-H
				2918-2850 Ali. C-H
				1676 C=N
				1583 N-H bending
				1525, 1348 N=O
				740 C-Cl
APUS20	457.5			3363 O-H streatching
				3088 Ar. C-H
				2924-2823 Ali. C-H
				1253 C-N ,1691 C=N
				1579 N-H bending
				1525, 1348 N=O
				1089 C-O
APUS21	428.52	427.5 (M-1)	8.2-7.0 (m,12H, Ar-H),	3049 Ar. C-H
			3.1 (s,1H, N-H),	2920-2862 Ali. C-H
			3.4 (s, 2H, CH_2-S),	1658 C=N
			2.3 (s, 3H, CH_3),	1598 N-H bending
			2.2 (d, 2H, CH_2),	1224 C-F
			2.1 (s,1H, C-H).	

The synthesized compounds have been tested for their antibacterial activity against Gram (+) bacteria (Staphylococcus aureus ATCC6538) and (Bacillus subtilis ATCC6633) and Gram (-) bacteria (Echerichia coli ATCC8739). The antimicrobial activity of the synthesized compounds has been evaluated by agar diffusion method (Zone of Inhibition).

Antibacterial activity

Table 5: Antibacterial evaluation of some synthesized compounds against gram (+) bacteria (Staphylococcus aureus), Gram (-) bacteria (Escherichia coli) using the agar diffusion method

Tested bacteria						
Compound Code	S. aureus(ATCC 6538)		B. subtilis(ATCC 6633)		E. Coli(ATCC 8739)	
	Zone of Inhibition (mm)	Activity Index (%)	Zone of Inhibition (mm)	Activity Index(%)	Zone of Inhibition (mm)	Activity Index(%)
APUS1	13.33	53.40	12.80	55.41	10.5	55.49
APUS2	18.21	72.95	17.96	77.74	15.66	82.09
APUS5	11.88	47.59	13.77	59.61	11.88	62.79
APUS7	14.75	59.09	14.01	60.64	9.99	52.80
APUS9	16.98	68.02	15.20	65.80	12.20	64.48
APUS11	17.10	68.50	14.88	64.41	12.38	65.43
APUS13	14.10	56.49	11.98	51.86	10.87	57.45
APUS15	19.33	77.44	18.66	80.77	16.72	88.37
APUS17	20.10	80.52	19.33	83.67	17.33	91.59
APUS18	16.22	64.98	15.05	65.15	14.70	77.69
APUS19	16.90	67.70	16.01	69.30	15.10	79.80
APUS21	17.33	69.43	15.99	69.22	15.22	80.44
Ciprofloxacin	24.96	100	23.10	100	18.92	100

RESULTS AND DISCUSSION

Chemistry

In the present study, it has been discussed that the synthesis of various dihydropyrimidine fused with benzimidazole moiety. In which o-phenylenediamine and chloroacetic acid react in acidic medium by nucleophilic addition reaction to form 2-chloro methyl Benzimidazole. **(1).** The substituted Chalcone **(2)** was synthesized by a claisan-schmidt condensation reaction. The condensation of an aromatic aldehyde with aromatic ketone having α- hydrogen in presence of a strong base to form α, β-unsaturated ketone i.e Chalcone is form. The substituted Chalcone react with thiourea by Michael reaction. It is also called 1,4 addition reaction. In which thiourea act as nucleophile attack on 4-positon of the α, β-unsaturated ketone and keto-enol tautomerism occurs and 4-substitutedphenyl-6-substitutedphenyl-4,5-dihydropyrimidine-2- thiol. **(3).** Benzimidazole **(1)** fused with substituted dihydropyrimidine-2-thiol **(3)** in presence of THF and form 2-((4-substituted phenyl-6-substituted phenyl pyrimidine-2-ylthio) methyl)-1H-benzo[d]imidazole. **(4)**

The synthesized compounds APUS1 – APUS21 were assigned by its spectral data (IR, NMR and mass spectra). The IR spectrum showed absorption bands in the range from 3300-3400 cm^{-1} ^{for} NH in Benzimidazole, 3025-3169 cm^{-1} for aromatic hydrogens, 1620-1695 cm^{-1} for C=N function. The 1H NMR spectra of compounds were studied in DMSO. The aryl hydrogen peaks were showed in the range 7-8.5 ppm. The CH_2-S showed a singlet peak around 3.3-5.5 ppm. The mass spectrum showed a corresponding molecular ion peak at m/z with respect to their molecular weights (Table 4).

Anti-bacterial activity

The newly synthesized title compounds APUS1 – APUS21 were evaluated for their antibacterial activity against Staphylococcus aureus, Bacillus subtilis, E. coli. The antibacterial activity of the tested compounds was assessed by zone of inhibition using agar well diffusion method. Ciprofloxacin was used as standard drug for comparison. (Table 5). From the data electron withdrawing group like Cl, F, Br having highest antibacterial activity. Compound APUS17, APUS15, APUS2, APUS21 show significant antibacterial activity. The compounds having electron donating group like CH_3, OCH_3, having moderate antibacterial activity. APUS9, APUS11 compounds show moderate activity and compounds APUS1, APUS5, APUS13 having low activity. This evidence confirmed that suitable functional groups on benzene ring were necessary for better antibacterial activities in drug design. Hence these results implied that electron with-drawing groups play important roles in the antibacterial activities of these tested Compound.

CONCLUSIONS

The research study reported efficient synthesis of new analogs of dihydropyrimidine-benzimidazole conjugation. All compounds were characterized by standard spectroscopic techniques and evaluation of the antibacterial activity of all new compounds was carried out and proved significant to moderate activity also the compounds showed good inhibitory activity.

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