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Design, Synthesis, Characterisation and Antimicrobial Evaluation of Some Substituted Dihydropyrimidinone Derivatives

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ABSTRACT

Dihydropyrimidinone nucleus is an important pharmacophore in medicinal chemistry. The synthesis of dihydropyrimidinone derivatives remains a main focus of modern drug discovery. In the present study, a series of novel dihydropyrimidinone derivatives have been synthesized via Biginelli reaction. The compounds were characterized by FT-IR, ^{1}H NMR analysis, ^{13}C NMR and MASS analysis. The compounds have been evaluated in-vitro for their antimicrobial activity against various strains of gram positive bacterial and fungal strains. The studies revealed that the newly synthesized derivatives exhibited moderate to good antibacterial and antifungal activity.

Keywords: Dihydropyrimidinones; Biginelli reaction; Antibacterial; Antifungal

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INTRODUCTION

Dihydropyrimidinone nucleus is an important pharmacophore in medicinal chemistry. The synthesis of novel pyrimidine derivatives remains a main focus of modern drug discovery. The versatility of newer generation pyrimidines would represent a fruitful pharmacophore for further development of better medicinal agents [1]. Since now, researchers have been attracted toward designing more potent pyrimidine derivatives having wide range of biological activity. Pyrimidine is the most important member of all the diazines as this ring system occurs widely in living organisms. Purines, uric acid, alloxan, barbituric acid and a mixture of anti-malarial and antibacterials also contain the pyrimidine ring [2]. In view of our observations and in continuance of our research work [3-7], we hereby report the synthesis of some imidazolidinone linked dihydropyrimidinone derivatives. This work made us understand the antibacterial and antifungal potency of newly synthesized dihydropyrimidinone derivatives. The synthetic pathway for the reported compounds is illustrated in Scheme 1. The key intermediate compound was biginelli compound, ethyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate.

Biginelli compound was synthesized by multi component reaction of condensation of urea, ethylacetoacetate and aromatic aldehyde in presence of ethanol using conc. hydrochloric acid as a catalyst. Reaction of ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate with hydrazine hydrate afforded 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbohydrazide derivative. Condensation of the carbohydrazide derivatives with various substituted aromatic aldehydes yielded 6-methyl-2-oxo-4-phenyl-*N*'-[substituted phenylmethylidene]-1,2,3,4-tetrahydropyrimidine-5-carbohydrazide derivatives. Schiff bases so formed were cyclised to imidazolidinone derivatives by condensation with glycine in presence of benzene and ethanol. The physicochemical data of the titled compounds are described in Table 1. Structures of the synthesized compounds were established based on the physico chemical and spectral data. (IR, ^{1}HNMR, ^{13}C NMR, MASS). In conclusion we have synthesized some potent imidazolidinone linked dihydropyrimidinone derivatives.

Table 1: Physicochemical properties of the synthesized compounds

S. No	Compound code	Molecular formula	Percentage yield(%w/w)	Melting Point (˚C)	Rf value
1	DHPVU3	$C_{22}H_{23}N_5O_6$	75%	195-200˚C	0.51
2	DHPVU4	$C_{23}H_{25}N_5O_7$	64%	205-210˚C	0.64
3	DHPVU9	$C_{22}H_{22}N_6O_7$	80%	180-182˚C	0.52
4	DHPVU1	$C_{22}H_{23}N_5O_5$	85%	205-210˚C	0.63
5	DHPVU7	$C_{22}H_{22}ClN_5O_5$	54%	190-195˚C	0.71
6	DHPVU8	$C_{22}H_{22}ClN_5O_5$	76%	200-204˚C	0.59
7	DHPVU10	$C_{24}H_{27}N_5O_7$	55%	195-200˚C	0.56
8	DHPVT3	$C_{22}H_{23}N_5O_5S$	75%	185-190˚C	0.62
9	DHPVT4	$C_{23}H_{25}N_5O_6S$	62%	185-192˚C	0.54
10	DHPVT5	$C_{22}H_{23}N_5O_5S$	56%	180-185˚C	0.53

MATERIALS AND METHODS

All the solvents and reagents were of analytical grade. Characterization of the compounds was carried out by determining melting point, FT-IR, ^{1}H-NMR, ^{13}C NMR, and Mass spectral analysis. Melting points were determined by open end capillary method and are uncorrected. The mobile phase used for developing the chromatogram was ethyl acetate: toluene (9:1). TLC spots were detected using iodine vapours. IR spectra were recorded on a JASCO 4100 FT-IR spectrometer using KBr pellet technique. ^{1}H NMR and ^{13}C NMR were recorded on a Brucker 500 MHz spectrometer using tetramethylsilane as standard. Chemical shifts were recorded in parts per million (ppm). Mass spectra were recorded on MS 2020 mass spectrometer [8,9].

EXPERIMENTAL WORK

Synthesis of Biginelli Compound

A mixture of 0.15 mole of urea, 0.1 mole of ethylacetoacetate and 0.1 mole of benzaldehyde were dissolved in 25 ml of ethanol along with 3 drops of conc. HCl and refluxed for one and half an hour. The reaction mixture was then poured into 100 ml ice cold water with stirring and left overnight at room temperature, filtered and dried. The products were recrystallised using ethanol.

Synthesis of Carbohydrazide Derivative

A mixture of 0.1 mole of biginelli compound and 0.1 mole of hydrazine hydrate were dissolved in 10 ml of ethanol along with 4 drops of conc. sulphuric acid and refluxed for 3 hours. The reaction mixture was then evaporated to obtain a residue which was further recrystallised from ethanol.

Synthesis of Schiff Bases

About 0.01 mole of hydrazido product and 0.01 mole of substituted aromatic aldehydes dissolved in ethanol along with 5 ml of glacial acetic acid were refluxed for 4-5 h. The reaction mixture was then poured into ice cold water in a beaker, filtered and dried. The precipitate was then recrystallised from ethanol.

Synthesis of Dihydropyrimidinone Derivatives

A mixture of Schiff base (0.01 mol) and glycine (0.01 mol) in a mixture of benzene and ethanol were refluxed for about 6-7 hours. After cooling, the mixture was poured into ice cold water, filtered and dried to afford the titled compounds. The precipitate was then recrystallised from ethanol (Scheme 1).

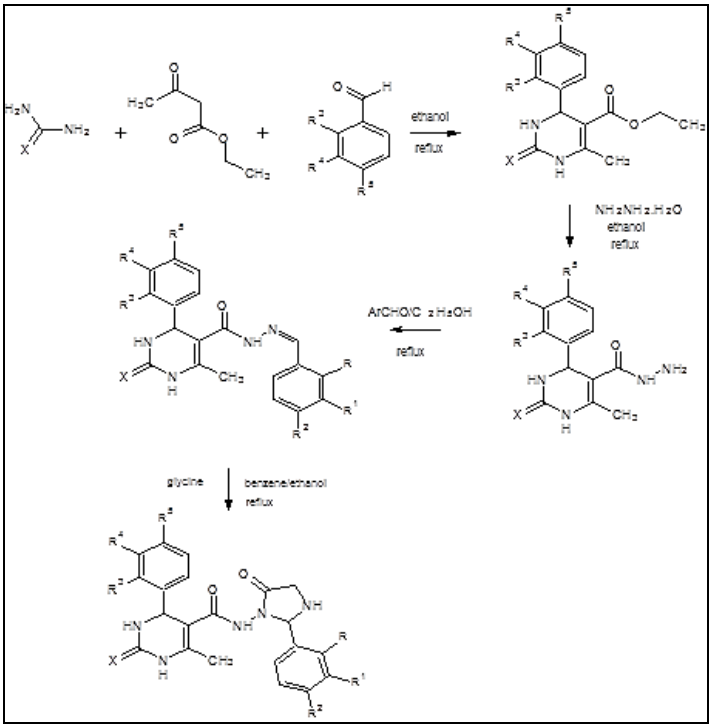
4-(4-hydroxy-3-methoxyphenyl)-N-(2-(2-hydroxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4 tetrahydropyrimidine-5-carboxamide(DHPVU3)

IR (KBr) cm^{-1}: 2922.92(NH stretching), 1695.31(C=O stretching), 1448.44(C-N stretching), 1020.27(C-O-C stretching), 2353.96(-OH stretching), 1650.95 (C=O stretching in amide),

^{1}H NMR (500 MHz, DMSO-d6, δppm): 9.115 (s, 1H, NH), 9.012 (s, 1H, NH), 8.921 (s, 1H, O=CNH), 3.728 (s, 3H, OCH_3), 1.131 (s, 3H, CH_3), 6.608-6.804 (m, 11H, Ar-H), 3.387 (s, 2H CH_2),

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.28 (C-OH), 56.05 (O-CH_3), 152.75(C-OCH_3), 148.40(C=O), 14.65(CH_3), 147.74(C-CH_3), 165.96(O=C-NH), 54.05(CH_2 of imidazolidinone ring), 159.15(C-OH), 136.42(C-phenyl ring), 115.77(2CH), 117.03(2CH),

MS: m/z: 451.15 $[M-2]^+$



Scheme 1: Synthesis of dihydropyrimidinone derivatives

S. No	Compound code	X	R	R^1	R^2	R^3	R^4	R^5
1	DHPVU3	O	OH	H	H	H	OCH_3	OH
2	DHPVU4	O	H	OCH_3	OH	H	OCH_3	OH
3	DHPVU9	O	NO_2	H	H	H	OCH_3	OH
4	DHPVU1	O	H	H	H	H	OCH_3	OH
5	DHPVU7	O	H	Cl	H	H	OCH_3	OH
6	DHPVU8	O	H	H	Cl	H	OCH_3	OH
7	DHPVU10	O	OCH_3	OCH_3	H	H	OCH_3	OH
8	DHPVT3	S	OH	H	H	H	OCH_3	OH
9	DHPVT4	S	OCH_3	OH	H	H	OCH_3	OH
10	DHPVT5	S	H	H	OH	H	OCH_3	OH

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-hydroxy-3-methoxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU4)

IR (KBr) cm^{-1}: 2907.49(Ar-H stretching), 1695.31(C=O stretching), 1516.91(C-N stretching), 1092.60(C-O-C stretching), 2851.56(-OH stretching), 1646.13 (C=O stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 8.922 (s, 1H, NH), 9.119 (s, 1H, NH), 7.639 (s,1H, O=CNH), 3.726 (s, 3H, OCH_3), 1.132 (s, 3H, CH_3), 6.62-6.802 (m, 10H, Ar-H), 4.018 (s,2H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.27 (C-OH), 56.04 (O-CH_3), 152.72(C-OCH_3), 148.39(C=O), 14.64(CH_3), 147.73(C-CH_3), 165.94(O=C-NH), 54.03(CH_2 of imidazolidinone ring), 136.40(C-phenyl ring), 115.75(2CH), 118.77(2CH), **MS: m/z:** 485.1 $[M+2]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(2-nitrophenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide(DHPVU9)

IR (KBr) cm^{-1}: 2922.92(Ar-H stretching), 3221.87(NH stretching), 1696.28(C=O stretching), 1452.30(C-N stretching), 1092.60(C-O-C stretching), 2851.56(-OH stretching), 1516.91(NO_2 stretching), 1646.13 (C=O stretching in amide),

^{1}H NMR (500 MHz, DMSO-d6, δppm): 9.118 (s, 1H, NH), 8.992 (s, 1H, OH), 8.917(s, 1H, NH), 7.635 (s,1H, O=CNH), 3.977 (s, 3H, OCH_3), 1.131 (s, 3H, CH_3), 6.611-7.882 (m, 11H, Ar-H), 4.019 (s,2H, CH_2),

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.30 (C-OH), 56.07 (O-CH_3), 152.78(C-OCH_3), 148.40(C=O), 14.66(CH_3), 147.76(C-CH_3), 165.98(O=C-NH), 54.07(CH_2 of imidazolidinone ring), 159.15(C-OH), 136.43(C-phenyl ring), 115.79(2CH), 118.80(2CH), 149.40(C-NO_2)

MS: m/z: 482.23$[M]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU1)

IR (KBr) cm^{-1}: 2923.88(Ar-H stretching), 3258.51(NH stretching), 1632.63(C=O stretching), 1366.47(C-N stretching), 1168.78(C-O-C stretching), 3112.89(-OH stretching), 1702.06 (C=O stretching in amide), 2993.88(NH stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 9.124 (s, 1H, OH), 8.880 (s, 1H, OH), 8.718 (s,1H, NH), 7.641(s,1H, O=CNH), 3.721 (s, 3H, OCH_3), 1.123 (s, 3H, CH_3), 6.605-6.801 (m, 12H, Ar-H), 4.012 (s,1H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.33 (C-OH), 59.70 (O-CH_3), 152.83(C-OCH_3), 148.45(C=O), 14.70(CH_3), 147.80(C-CH_3), 166.02(O=C-NH), 54.10(CH_2 of imidazolidinone ring), 136.46(C-phenyl ring), 115.82(2CH), 118.83(2CH)

MS: m/z: 435.30 $[M+2]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(3-chlorophenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU7)

IR (KBr) cm^{-1}: 3234.40(Ar-H stretching), 2923.88(NH stretching), 1703.03(C=O stretching), 1276.29(C-N stretching), 1092.60(C-O-C stretching), 1644.20 (C=O stretching in amide), 799.44(C-Cl stretching)

^{1}H NMR (500MHz, DMSO-d6, δppm): 9.119 (s, 1H, OH), 8.919 (s, 1H, NH), 7.636 (s,1H, O=CNH), 3.727 (s, 3H, OCH_3), 1.132 (s, 3H, CH_3), 6.606-6.805 (m, 11H, Ar-H), 4.019 (s,2H, CH_2)

^{13}C NMR (500MHz, DMSO-d6, δppm): 146.28 (C-OH), 56.05 (O-CH_3), 152.74(C-OCH_3), 148.39(C=O), 14.64(CH_3), 147.74(C-CH_3), 165.96(O=C-NH), 54.05(CH_2 of imidazolidinone ring), 136.42(C-Cl), 115.77(2CH), 118.78(2CH)

MS: m/z: 472.20 $[M+1]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-chlorophenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide(DHPVU8)

IR (KBr) cm^{-1}: 2920.99(Ar-H stretching), 3415.70(NH stretching), 1699.17(C=O stretching), 1271.97(C-N stretching), 1090.67(C-O-C stretching), 3175.64(-OH stretching), 796.58(C-Cl stretching), 1646.13 (C=O stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 8.950 (s, 1H, OH), 8.727(s, 1H, NH), 7.918 (s,1H, O=CNH), 3.725 (s, 3H, OCH_3), 1.131 (s, 3H, CH_3), 6.619-7.639 (m, 11H, Ar-H), 4.018(s,2H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.30 (C-OH), 56.05 (O-CH_3), 152.75(C-OCH_3), 148.40(C=O), 14.66(CH_3), 147.75(C-CH_3), 165.97(O=C-NH), 54.05(CH_2 of imidazolidinone ring), 136.41(C-Cl), 115.77(2CH), 118.78(2CH)

MS: m/z: 473.85$[M+2]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(2,3-dimethoxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU10)
IR (KBr) cm^{-1}: 2922.92(Ar-H stretching), 2849.63(NH stretching), 1708.81(C=O stretching), 1272.93(C-N stretching), 1092.60(C-O-C stretching), 2367.82(-OH stretching), 1645.17 (C=O stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 9.117 (s, 1H, OH), 8.924 (s, 1H, NH), 7.084(s,1H, O=CNH), 3.729 (s, 3H, OCH_3), 3.832 (s, 3H, OCH_3), 2.243(s, 3H, OCH_3), 1.132 (s, 3H, CH_3), 6.609-6.808 (m, 10H, Ar-H), 3.978 (s,2H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.29 (C-OH), 55.92 (O-CH_3), 56.06 (O-CH_3), 56.13 (O-CH_3), 152.76(C-OCH_3), 148.41(C=O), 14.66(CH_3), 147.75(C-CH_3), 165.97(O=C-NH), 54.06(CH_2 of imidazolidinone ring), 136.43(C-phenyl ring), 115.78(2CH), 118.79(2CH)

MS: m/z: 496.8 $[M-1]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(2-hydroxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVT3)
IR (KBr) cm^{-1}: 2998.14(Ar-H stretching), 3417.63(NH stretching), 1688.56(C=O stretching), 1373.22(C-N stretching), 1155.28(C-O-C stretching), 3176.54(-OH stretching), 796.58(C=S stretching), 1586.34 (C=O stretching in amide), 3121.57(NH stretching)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 10.256 (s, 1H, OH), 9.562 (s, 1H, OH), 9.017 (s, 1H, NH), 7.705 (s,1H, O=CNH), 3.733 (s, 3H, OCH_3), 1.135 (s, 3H, CH_3), 6.589-6.997 (m, 11H, Ar-H), 3.391 (s,2H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.65 (C-OH), 56.07 (O-CH_3), 145.12(C=O), 14.59(CH_3), 147.85(C-CH_3), 165.76(O=C-NH), 54.18(CH_2 of imidazolidinone ring), 135.07(C-OH), 115.90(2CH), 119.04(2CH), 174.54(C=S)

MS: m/z: 469.80 $[M]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-hydroxy-3-methoxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVT4)
IR (KBr) cm^{-1}: 2998.14(Ar-H stretching), 3415.70(NH stretching), 1688.56(C=O stretching), 1373.26(C-N stretching), 1111.89(C-O-C stretching), 3174.61(-OH stretching), 795.58(C=S stretching), 1586.34 (C=O stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 10.254 (s, 1H, OH), 9.561 (s, 1H, OH), 9.027 (s, 1H, NH), 3.732 (s, 3H, OCH_3), 1.137 (s, 3H, CH_3), 6.601-6.794 (m, 10H, Ar-H), 4.045(s,2H, CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.61 (C-OH), 56.03 (O-CH_3), 174.49(C=S), 14.55(CH_3), 147.80(C-CH_3), 165.72(O=C-NH), 54.13(CH_2 of imidazolidinone ring), 145.08(C-OH), 135.03(C-phenyl ring), 115.86(2CH), 111.38(2CH), **MS: m/z:** 498 $[M-1]^+$

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-hydroxyphenyl)-5-oxoimidazolidin-1-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVT5)
IR (KBr) cm^{-1}: 2998.14(Ar-H stretching), 3415.70(NH stretching), 1688.56(C=O stretching), 1373.26(C-N stretching), 1111.89(C-O-C stretching), 3175.64(-OH stretching), 795.58(C=S stretching), 1586.34 (C=O stretching in amide)

^{1}H NMR (500 MHz, DMSO-d6, δppm): 10.266 (s, 1H, OH), 9.570 (s, 1H, OH), 9.029 (s, 1H, NH), 3.732 (s, 3H, OCH_3), 1.136 (s, 3H, CH_3), 7.365(s,1H,O=CNH), 6.584-6.794 (m, 11H, Ar-H), 4.044 (s,2H,CH_2)

^{13}C NMR (500 MHz, DMSO-d6, δppm): 146.66 (C-OH), 56.07 (O-CH_3), 174.54(C=S), 14.59(CH_3), 147.85(C-CH_3), 165.77(O=C-NH), 54.18(CH_2 of imidazolidinone ring), 145.12(C-OH), 135.07(C-phenyl ring), 115.91(2CH), 119.05(2CH)

MS: m/z: 469.80 $[M]^+$

In-vitro Antimicrobial Activity [10,11]

The discs of 6 mm diameter impregnated with drug was dried in incubator and stored in refrigerator. Liquid culture of the bacteria in broth is flooded on a solid medium in a plate (Muller Hinton agar (or) nutrient agar). Alternatively, the culture plate may be sub cultured by the bacterial culture by swab. The discs are then placed on the plate and incubated overnight. The zone of inhibition around the disc was noted in Figure 1.

In-vitro Antibacterial Activity

The standardized inoculums were inoculated in the plates prepared earlier (aseptically) by dipping a sterile cotton swab in the inoculums and streaking the swab all over the surface of the medium 3 times rotating the plate through an angle of 60º after each application. Finally the swab was swabbed round the edge of the agar surface. Each Petri dish was divided into parts, in each part samples discs of 100 µg (discs are soaked overnight in sample solution) and standard Ciprofloxacin 10 µg were placed with the help of sterile forceps. The petri dishes were placed in the refrigerator at 4ºC or at room temperature for 1 h for diffusion and incubated at 37ºC for 24 h. The zone of inhibition produced by different samples was measured (Table 2).

Table 2: *In-vitro* antibacterial activity of the synthesized compounds

S.No	Compound code	*S.albus*	*M.luteus*	*C.glutamicum*	*B.lentus*
1	DHPVU3	10	14	15	19
2	DHPVU4	9	21	7	7
3	DHPVU9	0	7	10	10
4	DHPVU1	0	7	7	16
5	DHPVU7	7	10	7	10
6	DHPVU8	17	36	26	12
7	DHPVU10	8	8	8	8
8	DHPVT3	11	9	7	10
9	DHPVT4	9	12	9	10
10	DHPVT5	12	11	10	8
11	Standard	19	33	32	35

In-vitro Antifungal Activity

Similar procedure was followed for antifungal activity using standard Fluconazole 10 µg. The petri dishes were placed in the refrigerator at 4ºC or at room temperature for 1 h for diffusion and incubated at 28ºC for 48 h. The zone of inhibition produced by different samples was measured in Table 3 and Figure 2.

Table 3: *In-vitro* antifungal activity of the synthesized compounds

S.No	Compound code	*S.cerevisiae*	*A.fumigatus*	*C.albicans*	*M.gypseum*
1	DHPVU3	12	13	25	11
2	DHPVU4	8	14	16	14
3	DHPVU9	8	14	9	11
4	DHPVU1	0	12	19	15
5	DHPVU7	11	11	15	16
6	DHPVU8	20	14	22	20
7	DHPVU10	9	7	8	8
8	DHPVT3	9	7	8	10
9	DHPVT4	8	9	15	8
10	DHPVT5	6	0	0	8
11	Standard	31	32	34	31

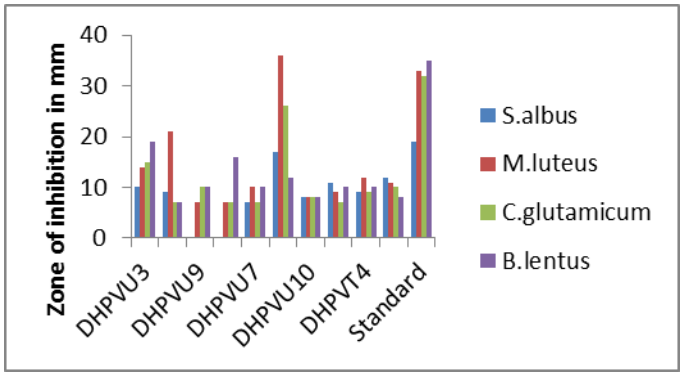


Figure 1: *In-vitro* antibacterial activity of the synthesized compounds

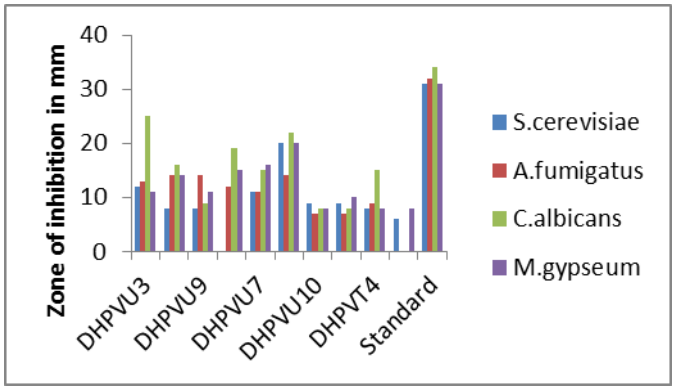


Figure 2: *In-vitro* antifungal activity of the synthesized compounds

RESULTS AND DISCUSSION

The titled compounds were synthesized in a four step process. The first step was synthesis of substituted dihydropyrimidinones by the condensation of urea and ethylacetoacetate with various substituted benzaldehydes in presence of an acid and ethanol, commonly known as Biginelli reaction. The advantage is that it is a useful intermediate to afford various medicinally important heterocyclic compounds. Dihydropyrimidinones were further condensed with hydrazine hydrate to afford carbohydrazide derivatives. The carbohydrazide derivatives of substituted dihydropyrimidines were finally condensed with various aromatic aldehydes to form the Schiff bases which were further cyclised with glycine in presence of benzene and ethanol to afford the target compounds. The melting points of all the titled compounds were reported. The melting points were determined in open capillary tubes with electrically heating melting point apparatus and are uncorrected. The solubility of all the synthesized compounds was checked by using the following solvents: Water, Benzene, Chloroform, Alcohol and DMSO. The purity of the all the titled compounds were checked by thin layer chromatography using silica gel as stationary phase, employing Ethyl acetate:Toluene (9:1) as mobile phase, spots was visualized using Iodine vapours. The Rf values of the synthesized compounds were also reported.

The infrared spectra of all the synthesized compounds were elucidated and expressed as wave number in cm^{-1}. The nuclear magnetic resonance spectra of synthesized compound were elucidated. The presence of CH_2 proton confirmed the formation of imidazolidinone ring and Mass spectral data was also found to be in correlation with the expected structure. The synthesized compounds were tested for antibacterial activity against gram positive bacteria such as *Streptococcus albus, Micrococcus luteus, Corynebacterium glutamicum and Bacillus lentus*. The zone of inhibition were measured and compared against a standard. The synthesized compounds were tested for antifungal activity against *Saccharomyces cerevisiae, Aspergillus fumigatus, Candida albicans* and *Microsporum gypseum*. The antibacterial and antifungal screening of all the compounds showed a moderate zone of inhibition than the standard.

CONCLUSION

Dihydropyrimidinones are therapeutically important class of compounds. The entitled work describes the synthesis of a series of substituted dihydropyrimidinone derivatives via Biginelli reaction. The purity of the compounds was established as single spot by Thin Layer chromatography. The structures of the compounds were elucidated by IR and ^{1}NMR, ^{13}C NMR, Mass spectral analysis. The synthesized compounds were screened for their *in-vitro* antimicrobial activity. The synthesized compounds were found to have a moderate antibacterial and antifungal activity. The present work details on the broad spectrum of antibacterial and antifungal activity in comparison with a standard antibiotic. It will be worthwhile to investigate the effect of titled compounds on other biological activities such as antitumor, anti HIV, antimalarial, antihypertensive etc., which can broaden the therapeutic utility for the compounds synthesized that will form part of a future study.

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