DESIGN, SYNTHESIS, CHARACTERISATION AND IN VITRO ANTIOXIDANT EVALUATION OF SOME SUBSTITUTED DIHYDROPYRIMIDINONE DERIVATIVES

Beena K. P.1*, Rajasekaran A.1, Manna P. K.2 and Suresh R.2

1Department of Pharmaceutical Chemistry, KMCH College of Pharmacy, Kalapatti Road, Coimbatore-48.
2Department of Pharmacy, Faculty of Engineering and Technology, Annamalai University, Annamalainagar, Tamilnadu.

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, 1H NMR analysis, 13C NMR and MASS analysis. The compounds have been evaluated in vitro for their antioxidant activity by DPPH method. The studies revealed that the newly synthesized derivatives exhibited significant antioxidant activity.

KEYWORDS: Dihydropyrimidinones, Biginelli reaction, antioxidant, DPPH method.

INTRODUCTION
Pyrimidine is the most important member of all the diazines as this ring system occurs widely in living organisms.[1] Purines, uric acid, alloxan, barbituric acid and a mixture of antimarial 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 antioxidant potency of newly synthesized dihydropyrimidinone derivatives.
The synthetic pathway for the reported compounds is illustrated in Scheme. 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 or thiourea, 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-carboxyldrazide derivative. Condensation of the carboxydrazide 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.

MATERIALS AND METHODS

All the solvents and reagents were of laboratory grade. Solvent system used for developing the chromatogram was ethyl acetate: toluene (9:1). TLC spots were detected using iodine vapours. 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 in open end capillary and are uncorrected. 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/thiourea, 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. Similar procedure was followed for various substituted aromatic aldehydes. The precipitate was then recrystallised from ethanol. The purity of the compounds was determined by thin layer chromatography.
Synthesis of carbohydrazido derivative
A mixture of 0.1 mole of biginelli compound and 0.1 mole of hydrazine hydrate were dissolved in 20 ml of ethanol along with 4 drops of conc. sulphuric acid and refluxed for 3 h. The reaction mixture was then evaporated to obtain a residue which was further recrystallised from ethanol. The purity of the compounds was determined by thin layer chromatography.

Synthesis of schiff bases of dihydropyrimidinone derivatives
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. The purity of the compounds was determined using thin layer chromatography.

Synthesis of dihydropyrimidinone derivatives
A mixture of Schiff base (0.01 mole) and glycine (0.01 mole) 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. The purity of the compounds was determined using thin layer chromatography.
Table 1 Physicochemical properties of the synthesized compounds

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound code</th>
<th>Molecular formula</th>
<th>Percentage yield (% w/w)</th>
<th>Melting Point (°C)</th>
<th>Rf value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>DHPVU3</td>
<td>C_{22}H_{23}N_{3}O_{6}</td>
<td>75%</td>
<td>195-200°C</td>
<td>0.51</td>
</tr>
<tr>
<td>2.</td>
<td>DHPVU4</td>
<td>C_{23}H_{24}N_{3}O_{7}</td>
<td>64%</td>
<td>205-210°C</td>
<td>0.64</td>
</tr>
<tr>
<td>3.</td>
<td>DHPVU9</td>
<td>C_{22}H_{22}N_{2}O_{7}</td>
<td>80%</td>
<td>180-182°C</td>
<td>0.52</td>
</tr>
<tr>
<td>4.</td>
<td>DHPVU1</td>
<td>C_{22}H_{22}N_{3}O_{3}</td>
<td>85%</td>
<td>205-210°C</td>
<td>0.63</td>
</tr>
<tr>
<td>5.</td>
<td>DHPVU7</td>
<td>C_{22}H_{22}ClN_{3}O_{5}</td>
<td>54%</td>
<td>190-195°C</td>
<td>0.71</td>
</tr>
<tr>
<td>6.</td>
<td>DHPVU8</td>
<td>C_{22}H_{22}ClN_{3}O_{5}</td>
<td>76%</td>
<td>200-204°C</td>
<td>0.59</td>
</tr>
<tr>
<td>7.</td>
<td>DHPVU10</td>
<td>C_{24}H_{24}N_{3}O_{7}</td>
<td>55%</td>
<td>195-200°C</td>
<td>0.56</td>
</tr>
<tr>
<td>8.</td>
<td>DHPVT3</td>
<td>C_{22}H_{22}N_{3}O_{5}S</td>
<td>75%</td>
<td>185-190°C</td>
<td>0.62</td>
</tr>
<tr>
<td>9.</td>
<td>DHPVT4</td>
<td>C_{23}H_{23}N_{3}O_{6}S</td>
<td>62%</td>
<td>185-192°C</td>
<td>0.54</td>
</tr>
<tr>
<td>10.</td>
<td>DHPVT5</td>
<td>C_{22}H_{23}N_{3}O_{5}S</td>
<td>56%</td>
<td>180-185°C</td>
<td>0.53</td>
</tr>
</tbody>
</table>

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(2-hydroxyphenyl)-5-oximidazolidin-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-d\(_6\), \(\delta\) ppm): 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\(_2\)), \(^1^3\)C NMR (500 MHz, DMSO-d\(_6\), \(\delta\) ppm): 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=CNH), 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]*.

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-hydroxy-3-methoxyphenyl)-5-oximidazolidin-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-d\(_6\), \(\delta\) ppm): 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 (500MHz, DMSO-d$_6$, δ ppm): 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$^2_2$ stretching), 1646.13 (C=O stretching in amide), $^1$H NMR (500MHz, DMSO-d$_6$, δ ppm): 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$_3$), 6.61-7.882 (m, 11H, Ar-H), 4.019 (s, 2H, CH$_2$), $^{13}$C NMR (500MHz, DMSO-d$_6$, δ ppm): 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), 54.03(CH$_2$ of imidazolidinone ring), 159.15(C-OH), 136.43(C-phenyl ring), 115.79(2CH), 118.80(2CH), 149.40(C-NO$^2_2$) MS: m/z: 485.1 [M+2]$^+$. 

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$^{-1}$: 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$^2_2$ stretching), 1646.13 (C=O stretching in amide), $^1$H NMR (500MHz, DMSO-d$_6$, δ ppm): 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, 12H, Ar-H), 4.012 (s, 1H, CH$_2$), $^{13}$C NMR (500MHz, DMSO-d$_6$, δ ppm): 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: 485.1 [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-d$_6$, δ ppm): 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-d$_6$, δ ppm): 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=CH$_3$), 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-o xoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU8)

IR(KBr)cm$^{-1}$: 2920.99(App-H stretching), 3415.70(NH stretching), 1699.17(C=O stretching), 1271.97(C-N stretching), 1109.67(C-O-C stretching), 3175.64(OH stretching), 796.58(C-Cl stretching), 54.05(CH$_2$ of imidazolidinone ring), 136.42(C-Cl), 115.78(2CH), 118.79(2CH), MS: m/z: 473.85[M+2]+.

1H NMR (500MHz, DMSO-d$_6$, δ ppm): 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$_2$), 13C NMR (500MHz, DMSO-d$_6$, δ ppm): 146.30 (C-OH), 56.05 (O-CH$_3$), 56.06 (O-CH$_3$), 148.39(C=O), 14.66(CH$_3$), 147.75(C-CH$_3$), 165.97(O=CH$_3$), 54.05(CH$_2$ of imidazolidinone ring), 136.42(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-o xoimidazolidin-1-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVU10)

IR(KBr)cm$^{-1}$: 2922.92(App-H stretching), 2849.63(NH stretching), 1708.81(C=O stretching), 1272.93(C-N stretching), 1105.28(C-O-C stretching), 2367.82(OH stretching), 1645.17(C=O stretching in amide), 1H NMR (500MHz, DMSO-d$_6$, δ ppm): 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$_3$), 13C NMR (500MHz, DMSO-d$_6$, δ ppm): 146.29 (C-OH), 56.05 (O-CH$_3$), 56.06 (O-CH$_3$), 148.41(C=O), 14.66(CH$_3$), 147.75(C-CH$_3$), 165.97(O=CNH), 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-o xoimidazolidin-1-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVT3)

IR(KBr)cm$^{-1}$: 2998.14(App-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=S stretching in amide), 3121.57(NH stretching), 1H NMR (500MHz, DMSO-d$_6$, δ ppm): 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\textsubscript{2}), \textsuperscript{13}C NMR (500MHz, DMSO-d\textsubscript{6}, δppm): 146.65 (C-OH), 56.07 (O-CH\textsubscript{3}), 145.12(C=O), 14.59(CH\textsubscript{3}), 147.85(C-CH\textsubscript{3}), 165.76(O=C-NH), 54.18(CH\textsubscript{2} of imidazolidinone ring), 135.07(C-OH), 115.90(2CH), 119.04(2CH), 174.54(C=S) \textbf{MS: m/z: 469.80 [M]+}.

4-(4-hydroxy-3-methoxyphenyl)-N-(2-(4-hydroxy-3-methoxyphenyl)-5-oxo imidazolidin-1-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (DHPVT4)

IR(KBr)cm\textsuperscript{-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), \textsuperscript{1}H NMR (500MHz, DMSO-d\textsubscript{6}, δppm): 10.254 (s, 1H, OH), 9.561 (s, 1H, OH), 9.027 (s, 1H, NH), 3.732 (s, 3H, OCH\textsubscript{3}), 1.137 (s, 3H, CH\textsubscript{3}), 6.601-6.794 (m, 10H, Ar-H), 4.045(s,2H, CH\textsubscript{2}), \textsuperscript{13}C NMR (500MHz, DMSO-d\textsubscript{6}, δppm): 146.61 (C-OH), 56.03 (O-CH\textsubscript{3}), 174.49(C=S), 14.55(CH\textsubscript{3}), 147.80(C-CH\textsubscript{3}), 165.72(O=C-NH), 54.13(CH\textsubscript{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\textsuperscript{-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), \textsuperscript{1}H NMR (500MHz, DMSO-d\textsubscript{6}, δppm): 10.266 (s, 1H, OH), 9.570 (s, 1H, OH), 9.029 (s, 1H, NH), 3.732 (s, 3H, OCH\textsubscript{3}), 1.136 (s, 3H, CH\textsubscript{3}), 7.365(s,1H,O=CNH), 6.584-6.794 (m, 11H, Ar-H), 4.044 (s,2H,CH\textsubscript{2}), \textsuperscript{13}C NMR(500MHz, DMSO-d\textsubscript{6}, δppm): 146.66 (C-OH), 56.07 (O-CH\textsubscript{3}), 174.54(C=S), 14.59(CH\textsubscript{3}), 147.85(C-CH\textsubscript{3}), 165.77(O=C-NH), 54.18(CH\textsubscript{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]+.

**INVITRO ANTIOXIDANT ACTIVITY**

**DPPH radical scavenging assay**

The reaction is based on the reduction of 1,1-diphenyl-2-picrylhydrazyl, which is a stable free radical. DPPH on reaction with a substance that can donate a hydrogen atom, this gives rise to the reduced form with the loss of violet colour; pale yellow colour remains from the picryl group. Various concentrations of sample (20, 40, 60, 80, 100µg/ml) and the reference compound were prepared in 0.3mM solution of DPPH in ethanol. The mixture was shaken vigorously and allowed to stand in dark at room temperature for 30 min. Then the absorbance was measured at 517 nm against a blank. Reference compound used was ascorbic acid. The
percentage of inhibition was calculated by comparing the absorbance values of the control and test samples. The percentage of inhibition was calculated using the following equation:

**Percentage inhibition (I %) = \( \frac{(A_{\text{control}} - A_{\text{sample}})}{A_{\text{control}}} \times 100 \)**

Where ‘\( A_{\text{control}} \)’ was the absorbance of the control and ‘\( A_{\text{sample}} \)’ was the absorbance of the sample. The antioxidant activity of the compounds was expressed as IC\(_{50} \). (IC\(_{50} \) - concentration required to obtain a 50% radical scavenging activity). The results are tabulated in Table no.2.

**Table no. 2 Invitro antioxidant activity of the synthesized compounds**

<table>
<thead>
<tr>
<th>Compound code</th>
<th>Concentration (µg/ml)</th>
<th>IC(_{50}) (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>DHPVU3</td>
<td>24.95</td>
<td>31.48</td>
</tr>
<tr>
<td>DHPVU4</td>
<td>21.45</td>
<td>38.49</td>
</tr>
<tr>
<td>DHPVU9</td>
<td>24.99</td>
<td>43.78</td>
</tr>
<tr>
<td>DHPVU1</td>
<td>ND</td>
<td>19.38</td>
</tr>
<tr>
<td>DHPVU7</td>
<td>20.83</td>
<td>32.93</td>
</tr>
<tr>
<td>DHPVU8</td>
<td>23.98</td>
<td>41.74</td>
</tr>
<tr>
<td>DHPVU10</td>
<td>21.72</td>
<td>37.75</td>
</tr>
<tr>
<td>DHPVT3</td>
<td>31.93</td>
<td>54.67</td>
</tr>
<tr>
<td>DHPVT4</td>
<td>26.82</td>
<td>39.28</td>
</tr>
<tr>
<td>DHPVT5</td>
<td>33.81</td>
<td>52.73</td>
</tr>
<tr>
<td>Standard</td>
<td>24.93</td>
<td>43.16</td>
</tr>
</tbody>
</table>

Each value is expressed as percentage of activity mean ± standard deviation (n=3)
ND- Not Detected.

**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 or thioureaacetate 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 carbohydrazido derivatives. The carbohydrazido derivatives of substituted dihydropyrimidines were finally condensed with various aromatic aldehydes to afford the Schiff bases which was 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. Most of the synthesized compounds exhibited pronounced antioxidant activity.

**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 *invitro* antioxidant activity. The synthesized compounds were found to have a significant activity. The present work details on the broad spectrum of antioxidant activity in comparison with a standard.

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.

**REFERENCES**

2. T.L. Lemke, D.A. Williams, V.F. Roche, S.W. Zito, Wolters kluwer, New Delhi, 2008; 6$^{th}$ edn., 117-120.


