FULL PAPER

Anti-cancer and antioxidant activities of some new synthesized 3-secondary amine derivatives bearing imidazo [1,2-A] pyrididine

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In this study, new series of 2-aryl-3-(pyrimidine-2-ylamino)imidazo[1,2-a]pyrimidine derivatives (3-secondary amine) were synthesized through one-pot reaction of aromatic ketones and 2-aminopyrimidine. These reactions were performed in the presence of I2 and DMSO. Derivatives of 3-amine compound were reacted with propargyl bromid to yield 2-phenyl-N-(prop-2-yn-1-yl)-N-(pyrimidine-2-yl) derivatives of imidazo/pyrimidine rings. Then, by Mannich reaction, one of 3-secondary amine derivatives (contains NH2 group) (1d) was reacted with different aromatic amines to form Mannich bases. All synthesized compounds were characterized via FT-IR spectroscopy, some of which were characterized by 1H-NMR spectroscopy. Other derivatives of imidazo(1,2-a)pyrimidine(1c,2c,2d,3a) were evaluated for anti-oxidant activity and one of these derivatives (2d) was tested for cytotoxic activity against breast cancer using MTT assay.

KEYWORDS
Imidazo[1,2-a]pyrimidine; one-pot reaction; anti-oxidant; MTT assay.

Introduction

Heterocyclic compounds that contain a bridge of nitrogen atom are of great importance in medical chemistry and industrial applications as anti-corrosion. Imidazo[1,2-a]pyrimidines are a prevalent and important fused heterocyclic system containing three nitrogen atoms and demonstrate structural similarities with purines [1]. Imidazo(1,2-a)pyrimidines are widespread structural motifs in pharmaceutically and biologically active compounds [2]. They have also been used in other applications such as azo dyes[3], fabric whiteners [4], anticonvulsant and anxiolytic activity [5]. To further explore their applications, their scaffold also acts as organic fluorophore used as biomarkers and photochemical sensors [6]. Also, some imidazo[1,2-a]pyrimidine derivatives have been reported to have significant anti-inflammatory and analgesic actions in experimental animal models[7,8]. Furthermore, The structural unit of imidazo[1,2-a]pyrimidines has been also found in a number of investigational drugs, such as divaplon, taniplon and fasiplon[9](Figure 1).

One of the most important reactions in organic chemistry is one-pot reaction. This type of reaction is widely used in organic synthesis to prevent separation and purification processes and thus obtain a large reaction yield in the shortest possible time. Many steps of bond- forming and chemical transformation can be accomplished by one-
pot reaction [10]. Recently, one-pot reaction has been used for synthesis of 2,3-disubstituted imidazo[1,2-a]pyridine by the reaction of 2-aminopyridine with different substituted acetophenone in the presence of DMSO and I$_2$ [11]. In this work, 2,3-disubstituted imidazo[1,2-a]pyrimidine (3-secondary amine) (DIP) was prepared using the abovementioned method. On the other hand, propargylamines were synthesized by the reaction of DIP derivatives with propargylbromide. Propargylamines are widely used in organic synthesis to form diverse heterocyclic compounds [12], natural products and bioactive compounds [13-15]. These compounds have a significant role in many pharmaceutical and biological applications, such as anti-cancer [16], antibacterial [17], anti-fungal [18], antiproliferative [19]. Conventional methods of synthesis of propargylamines involve amination of propargylic halides, phosphates, or triflates [20-22] and reaction of lithium acetylides or Grignard reagents with imines or their derivatives [23,24].

![structures of some drugs that contain imidazo[1,2-a]pyrimidine core](image)

In addition, the synthesis of Mannich bases can be performed by the reaction of one of the DIP derivatives with different amines. These compounds were synthesized by Mannich reaction that is a widely used reaction to the production of new drugs and as a key reaction for the development of biological active compounds [25]. Mannich bases show a wide variety of biological and pharmaceutical activities as the final product of the Mannich reaction such as antifamatory [26], antibacterial [27], antitumor [28], antioxidant [29], anti-fungal [30].

The aim of the research was to synthesize new compounds of imidazo[1,2-a]pyrimidine and study their activities as anticancer and antioxidant.

**Materials and methods**

**Experimental instruments**

A. Melting point was recorded using electro thermal melting point apparatus.

B. All the (1H and 13C NMR) spectra were recorded on bruker ultra-shield 500MHz spectrometer using DMSO$_d$6 as solvent as an internal standard.

C. Chemical shift values are listed in δ scale

The IR spectra were recorded on Schimidzu FTIR spectro photometer by using 1% potassium bromide discs.

**Synthesis of 2-Aryl-3-(pyrimidine-2-ylamino)imidazo[1,2-a]pyrimidine (General procedure (1a))**

A mixture of acetophenone (0.0026 mol) and I$_2$ (2 mL, 0.0026 mol) in DMSO (5 mL) was heated under reflux at 100°C for 6 hours. After that, 2-aminopyrimidine(0.0052 mol) was added and then heated for an additional 2 hours. The resulting solution was cooled and poured in crushed ice. The formed precipitate was filtered and recrystallized from ethanol to obtain compound (1a).

Elemental analysis was as follows: C$_{16}$H$_{12}$N$_6$. IR(KBr/cm$^{-1}$): 3159(N-H), 3037(Ar-H), 1614(C=N)imidazo, 1575(C=N)pytimidine, 1560(C=C). $^{1} $H-NMR (DMSO, 500 MHz) δ: 6.87-8.83(m,Ar-H, s, 1H,NH ), $^{13}$C-NMR (DMSO, 500 MHz) δ: 169.3-138.8(C=N), 138.6-115.3(C=C).
2-(4-Bromophenyl)-3-(pyrimidine-2-ylamino)imidazo(1,2-a)pyrimidine (1b)

Elemental analysis was as follows: C_{16}H_{11}BrN_{6}: IR(KBr/cm\textsuperscript{-1}): 3110(N-H), 3078(Ar-H), 1641(C=N)imidazo, 1614(C=N)pyrimidine, 1537(C=C), 744(C-Br). \textsuperscript{1}H-NMR (DMSO, 500 MHz) δ: 6.75-8.77 (m, Ar-H, s,1H,NH), \textsuperscript{13}C-NMR (DMSO, 500 MHz) δ: 168.5-148.3(C=N), 136.6-115.3(C=C).

2-(4-Nitrophenyl)-3-(pyrimidine-2-ylamino)imidazo(1,2-a)pyrimidine (1c)

Elemental analysis was as follows: C_{16}H_{11}N_{2}O_{2}: IR(KBr/cm\textsuperscript{-1}): 3224(NH), 3074(Ar-H), 1633(C=C). \textsuperscript{1}H-NMR (DMSO, 500 MHz) δ: 8.48 (s, OH), 5.37(s, 2H,NH). \textsuperscript{13}C-NMR (DMSO, 500 MHz) δ: 165.3-147.4(C=N), 137.1-108.3(C=C).

2-(4-Hydroxyphenyl)-3-(pyrimidine-2-ylamino)imidazo(1,2-a)pyrimidine (1e)

Elemental analysis was as follows: C_{16}H_{12}N_{7}: IR(KBr/cm\textsuperscript{-1}): 3415(OH), 3103(NH), 3014(Ar-H), 2954(C≡C), 1616(C=N)imidazo, 1560(C=N)pyrimidine, 1583(C=C); \textsuperscript{1}H-NMR (DMSO, 500 MHz) δ: 8.83-6.86 (m, Ar-H, s, 1H, NH), 9.67 (s, OH). \textsuperscript{13}C-NMR (DMSO, 500 MHz) δ: 169.3-148.6 (C=N, C-OH), 138.6-109.6(C=C).

TABLE 1 Physical properties of compounds (1a-e)

<table>
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<tr>
<th>Com.No.</th>
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<th>M.F.</th>
<th>M.P.(C\textdegree)</th>
<th>Color</th>
<th>Yield(%)</th>
</tr>
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<td>65</td>
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**Synthesis of propargylamines (2a-e)(General procedure)**

2-Phenyl-N-(prop-2-yn-1-yl)-N-(pyrimidine-2-ylamino)imidazo(1,2-a)pyrimidine (2a):

To a mixture of compound (1a 0.02 mol) and K_{2}CO\textsubscript{3} (0.01 mol) in DMF (25 mL) solvent, the propargylbromide (1 mL) was added at room temperature. The reaction mixture was refluxed for 5 hours. After the reaction ended, the reaction mixture was poured into crushed ice and stirred for 15 minutes. The formed precipitate was filtered and recrystallized from chloroform to obtain compound (2a).

Another synthesis was as follows: C_{19}H_{14}N_{6}: IR(KBr/cm\textsuperscript{-1}): 3277(C\equiv C-H), 2165(C\equiv C), 1598(C=N)imidazo, 1583(C=N)pyrimidine, 1514(C=C); \textsuperscript{1}H-NMR (DMSO,500 MHz) δ: 8.33-6.67 (m, Ar-H), 4.67(s,2H,CH\textsubscript{2}), 3.08(s,1H, C\equiv C-H). \textsuperscript{13}C-NMR (DMSO, 500 MHz) δ: 167.3-148.4(C=N), 138.6-115.3(C=C), 78, 73(C\equiv C), 43.3(CH\textsubscript{2}).
2-(4-Bromophenyl)-N-(prop-2-yn-1-yl)-N-(pyrimidine-2-ylamino)imidazo[1,2-a]pyrimidine (2b)

Elemental analysis was as follows: C_{19}H_{13}BrN_{6}.

IR(KBr/cm⁻¹): 3245(C≡C), 1616(C≡N)imidazo, 1575(C=N)pyrimidine, 1556,1514(C=C).
{^1}H-NMR (DMSO,500 MHz) δ: 8.43-6.95(m, Ar-H), 4.47(s.2H,CH₂), 3.2(s,1H, C≡C-H), 13^{13}C-NMR (DMSO, 500 MHz) δ: 168.2-147.3(C≡C), 138.7-109.4(C=C), 78.4,73.1(C≡C), 43.3(CH₂).

2-(4-Nitrophenyl)-N-(prop-2-yn-1-yl)-N-(pyrimidine-2-ylamino)imidazo[1,2-a]pyrimidine (2c)

Elemental analysis was as follows: C_{19}H_{13}N_{6}O:

IR(KBr/cm⁻¹): 3224(C≡C), 1656,1514(NO₂). {^1}H-NMR (DMSO,500 MHz) δ: 8.83-6.87(m, Ar-H), 4.67(s, 2H, CH₂), 2.9(s, 1H, C≡C-H), 13^{13}C-NMR (DMSO, 500 MHz) δ: 167.1-149.3(C≡C), 137.3-109.7(C=C), 77.2,73.3(C≡C).

Synthesis of Mannich bases (3a-j) (General procedure)
A Mannich bases were synthesized by adding of (1d) compound, formaldehyde and differentamines in an equimolar ratio as one-pot reaction. Amixture of (1d) (0.001 mol), 37% formaldehyde (0.001 mol) and primary or secondary amines (0.001 mol) in absolute

<table>
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<th>Com.No.</th>
<th>R</th>
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<th>Yield(%)</th>
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TABLE 2 Physical properties of compounds (2a-e)
ethanol was refluxed for 12 hours. After the reflux stopped, the reaction mixture was allowed to cool at room temperature and the solid mass obtained was filtered, dried and recrystallized from absolute ethanol. Physical properties of compounds (3a-j) are shown in Table 3.

N-(2-Methoxy-4-nitrophenyl)-N-(4-(3-(pyrimidin-2-ylamino)imidazo[1,2-a]pyrimidin-2-yl)phenyl)methanedi amine (3a)

Elemental analysis was as follows: C_{24}H_{22}N_{10}O_{3} : IR(KBr/cm⁻¹): 3404, 3371 and 3301(NH), 2920 and 2893(CH aliphatic), 1654(C=N)imidazo, 1496 and 1452(C=C), 1521(NO₂). ¹H-NMR (DMSO, δ 00 MHz): 8.83-6.51(m, Ar-H), 6.34, 5.8(s,2H,CH₂), 3.9(s,3H,CH₃). ¹³C-NMR (DMSO, 500 MHz) δ: 167.4-149.1(C=N), 138.6-108.1(C=C), 70.4(CH₂), 55.1(CH₃).

N-(4-Chlorophenyl)-N-(4-(3-(pyrimidin-2-ylamino)imidazo[1,2-a]pyrimidin-2-yl)phenyl)methanedi amine (3d)

Elemental analysis was as follows: C_{23}H_{19}ClN_{8} : IR(KBr/cm⁻¹): 3417, 3359 and 3317(NH), 2974 and 2887(CH aliphatic), 1656(C=N)imidazo, 1517 and 1475(C=C). ¹H-NMR (DMSO, δ 00 MHz): 8.77-6.53(m, Ar-H), 8.47 and 6.34(3 singlets, 3NH), 4.79(s,2H,CH₂). ¹³C-NMR (DMSO, δ 00 MHz) δ: 165.3-146.6(C=N), 136.2-107.4(C=C), 68.5(CH₂).

N-(2-Nitrophenyl)-N-(4-(3-(pyrimidin-2-ylamino)imidazo[1,2-a]pyrimidin-2-yl)phenyl)methanedi amine (3e)

Elemental analysis was as follows: C_{23}H_{16}N_{10}O_{2} : IR(KBr/cm⁻¹): 3473, 3411 and 3392(NH), 2975 and 2887(CH aliphatic), 1654(C=N)imidazo, 1494 and 1445(C=C), 1521(NO₂). ¹H-NMR (DMSO, δ 00 MHz): 8.83-6.51(m, Ar-H), 6.34-5.8(s,2H, NH), 4.84(s,2H, CH₂). ¹³C-NMR (DMSO, δ 00 MHz) δ: 168.2-147.3(C=N), 146.7-109.5(C=C), 69.1(CH₂).

N-(3-Nitrophenyl)-N-(4-(3-(pyrimidin-2-ylamino)imidazo[1,2-a]pyrimidin-2-yl)phenyl)methanedi amine (3f)

Elemental analysis was as follows: for C_{23}H_{18}N_{10}O_{2}: IR(KBr/cm⁻¹): 3267,3207,3109(NH), 1676(C=O),1645(C=N)imidazo, 1614(C=N)pyrimidine,1583,1539,1498 and 1479(C=C). ¹H-NMR (DMSO, δ 00 MHz): 9.78(HN-C=O) 8.78-6.56(m, Ar-H), 6.34 and 5.77(s, 2H, NH), 2.1(s, 3H, CH₃). ¹³C-NMR (DMSO, 500 MHz) δ: 167.3-149.1(C=N, C=O), 147.6-109.1(C=C), 70.1(CH₂), 24.01(CH₃).
N-(Benzo[d]thiazol-2-yl)-n-[4-(3-{pyrimidin-2-ylamino}imidazo[1,2-a]pyrimidin-2-yl)phenyl]methandiamine (3g)

Elemental analysis was as follows: C_{24}H_{21}N_{9}O: IR (KBr/cm⁻¹): 3456 and 3427(NH), 2947 and 2883(CH aliphatic), 1616(C=N)imidazo, 1514 and 1438(C=C), 765(C-S-C) . ¹H-NMR (DMSO, 500 MHz) δ: 8.83-6.7(m, Ar-H), 6.34-5.9(s, 2H, NH), 4.83(s, 2H, CH₂). ¹³C-NMR (DMSO, 125 MHz) δ: 169.1-148.3(C=N), 147.2-108.3(C=C), 69.3(CH₃).

N-(4-Methoxyphenyl)-N-[4-(3-{pyrimidin-2-ylamino}imidazo[1,2-a]pyrimidin-2-yl)phenyl]methandiamine (3h)

Elemental analysis was as follows: C_{24}H_{22}N_{8}O: IR (KBr/cm⁻¹): 3411, 3392 and 3238(NH), 2975 and 2887(CH aliphatic), 1654(C=N)imidazo, 1521 and 1446(C=C), 1176(C=O-C). ¹H-NMR (DMSO, 500 MHz) δ: 8.73-6.51(m, Ar-H), 6.34(s, 2H, NH), 4.83(s, 2H, CH₂), 3.81(s, 3H, CH₃). ¹³C-NMR (DMSO, 125 MHz) δ: 167.1-146.3(C=N), 138.3-108.3(C=C), 96.2(CH₂).

N-[4-(3-{Pyrimidin-2-ylamino})imidazo[1,2-a]pyrimidin-2-yl]phenyl]-N-(p-tolyl)methandiamine (3i)

Elemental analysis was as follows: C_{24}H_{22}N_{8}: IR(KBr/cm⁻¹): 3429, 3394 and 3261(NH), 2989 and 2887(CH aliphatic), 1654(C=N)imidazo, 1523 and 1492(C=C). ¹H-NMR (DMSO, 500 MHz) δ: 8.76-6.45(m, Ar-H), 6.23(s, 2H, NH), 4.77(s, 2H, CH₂), 2.32(s, 3H, CH₃). ¹³C-NMR (DMSO, 125 MHz) δ: 169.3-149.1(C=N), 138.1-108.3(C=C), 68.3(CH₂), 21.3(CH₃).

N-[4-(3-{Pyrimidin-2-ylamino})imidazo[1,2-a]pyrimidin-2-yl]phenyl]-N-(o-tolyl)methandiamine (3j)

Elemental analysis was as follows: C_{24}H_{22}N_{8}: IR (KBr/cm⁻¹): 3407, 3367 and 3315(NH), 2952 and 2981(CH aliphatic), 1650(C=N)imidazo, 1510 and 1444(C=C). ¹H-NMR (DMSO, 500 MHz) δ: 8.73-6.51(m, Ar-H), 6.34-5.8(s, 2H, NH), 4.79(s, 2H, CH₂), 2.01(s, 3H, CH₃). ¹³C-NMR (DMSO, 125 MHz) δ: 167.7-147.8(C=N), 189.1-109.3(C=C), 96.2(CH₂).

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TABLE 3 Physical properties of compounds (3a-j)

<table>
<thead>
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<th>Com.No.</th>
<th>R</th>
<th>M.F</th>
<th>M.P.(C°)</th>
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<th>Yield (%)</th>
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Results and discussion

One-pot reaction was performed for synthesis 2-aryl-3-(pyrimidine-2-ylamino)imidazo[1,2-a]pyrimidine derivatives (1a-1e) from the reaction of 2-aminopyrimidine with different substituted acetophenones in the presence of I2 and DMSO (Scheme 1). These compounds were identified by the absence of the characteristic bands in the FT-IR spectrum for one carbonyl group and one NH2 group and the appearance of new peaks at (1600-1650 cm⁻¹) for (C=N) imidazo and at (3100-3300 cm⁻¹) for (NH) group. ¹HNMR spectrum showed multiple signals for (Ar-H, NH) protons at (8.83-6.5 ppm) and for (s, 1H, OH) protons at (9.67 ppm). Also, the synthesis of these compounds were identified by ¹CNMR spectrum that showed signals at 169.3-147.1 ppm (C=N) and at 138.1-109.3 ppm (C=C).

The second step was the synthesis of propargylamines by the reaction of (1a-1e) compounds with propargylbromide as SN₂ reaction (Scheme 2). The absorption characteristic peaks of these compounds in the FT-IR spectrum were at (2183-2133 cm⁻¹) owing to (C≡C) and at (3277-3224 cm⁻¹) owing to (C≡C-H). ¹HNMR signals at 2.9-3.2 ppm (s, 1H, C≡C-H). ¹CNMR showed new signals at 79-71 ppm(C≡C), 43.3 ppm(CH2).
SCHEME 2 The possible mechanism of formation of compounds (2a-2e)

On the third step, Mannich’s reaction was performed to form Mannich bases by the reaction of (1d) compound with different substituted aromatic amines in the presence of formaldehyde (37%). The FT-IR spectrum of these compounds showed new peaks at (3400-3100 cm⁻¹) for (NH) groups and at (3000-2800 cm⁻¹) owing to (CH₂), also the appearance of ¹HNMR signals at 4.9-4.1ppm for (s, 2H, CH₂), for all synthesized Mannich bases.

SCHEME 3 synthesis mechanism of compounds (3a-3j)

Cytotoxic effect of (2d) compound on MCF-7 cancer cell line using MTT assay

The test of 3-(dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) was accomplished to evaluate the cytotoxic effect of (2d) compound on breast cancer cell line (MCF-7). MTT assay was performed to calculate the cell viability and inhibition rate on the tumor cell line by using different concentrations of (2d) compound. The
percentage viability of treated cells was calculated in a comparison to normal cell line WPL-68. The cytotoxic effect of (2d) compound in concentration ranged from 6.25-400 μg/mL on MCF-7 cells (Table 4), which presented a decrease in cell viability in a dose-dependent pattern. The cell viability was reduced by increasing the concentration of (2d) compound. The decreasing in MCF-7 cell viability (%) was noticed at 400μg/mL (43.842±3.41%) while the highest MCF-7 cell viability at 6.25 μg/mL reached (94.791±1.64%). A (2d) compound exhibited cytotoxic activity with IC50 value of 96.37 μg/mL. However, an IC50 of 230.1 μg/mL was obtained from the effect of (2d) compound on WRI-68 normal cell line (Figure 2).

**TABLE 4** Cytotoxicity effect of (2d) compound on MCF-7 and WRI-68 cells after 24 hours incubation at 37 °C

<table>
<thead>
<tr>
<th>Concentration of (2d) compound μg/mL</th>
<th>Viable cell count of MCF-7 cell line Mean ± SD</th>
<th>Viable cell count of WRI-68 cell line Mean ± SD</th>
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<td>6.25</td>
<td>94.791 ± 1.64</td>
<td>95.023 ± 0.8349</td>
</tr>
</tbody>
</table>

**FIGURE 2** Cytotoxic effect of (2d) compound on MCF-7 and WRL-68 cells after 24 hours incubation at 37 °C.

**DPPH radical scavenging activity**

All tested samples possessed DPPH scavenging activity in a dose dependent manner. For sample (2d), it showed DPPH scavenging activity ranging from (15.5±3.8 to 74.81±2.9 %) for (12.5 to 100 mg/mL), respectively, with IC50 value of (22.48 mg/mL), while sample (2c) possessed DPPH scavenging activity ranging from (15.51±3.74 to 68.17±0.9 %) for (12.5 to 100 mg/mL), respectively, with IC50 value of (127.3 mg/mL). On the other hand, DPPH scavenging activity range of sample (1c) appeared from (10.27±1.59 to 38.65±3.57 %) for (12.5 to 100 mg/mL), respectively, with IC50 value of (377.4 mg/mL). Finally, sample (3a) showed DPPH scavenging activity ranging from (13.13±5.76 to 58.29±8.63 %) for (12.5 to 100 mg/mL), respectively, with IC50 value of (162 mg/mL). Vitamin C shows a strongest DPPH radical scavenging activity ranging from (24.89±4.96 to 85±2.6 %) for (12.5 to 100 mg/mL), respectively, with IC50 value of (34 mg/mL).
TABLE 1 DPPH Radical Scavenging Activity (Mean ± SD %)

<table>
<thead>
<tr>
<th>Concentration (mg/mL)</th>
<th>Sample (2d)</th>
<th>Sample (2c)</th>
<th>Sample (1c)</th>
<th>Sample (3a)</th>
<th>Vitamin C IC₅₀(34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>74.81±2.9</td>
<td>68.17±0.9</td>
<td>38.65±3.57</td>
<td>58.29±2.97</td>
<td>85±2.6</td>
</tr>
<tr>
<td>50</td>
<td>56.57±12.2</td>
<td>50.07±8.66</td>
<td>24.94±3.12</td>
<td>39.81±8.63</td>
<td>71.27±3.22</td>
</tr>
<tr>
<td>25</td>
<td>38.35±3.84</td>
<td>12.93±1.43</td>
<td>10.33±2.78</td>
<td>12.58±3.95</td>
<td>39.26±5.52</td>
</tr>
<tr>
<td>12.5</td>
<td>15.5±3.8</td>
<td>15.51±3.74</td>
<td>10.27±1.59</td>
<td>13.13±5.76</td>
<td>24.89±4.96</td>
</tr>
</tbody>
</table>

**FIGURE 3** DPPH scavenging activity of compound (2D) compared with vitamin C

**FIGURE 4** DPPH scavenging activity of compound (2C) compared with vitamin C

**FIGURE 5** DPPH scavenging activity of compound (1C) compared with vitamin C
Conclusion

In this work, a variety of imidazo[1,2-a]pyrimidine derivatives have been synthesized from 2-aminopyrimidine and different substituted acetoophenones. The newly synthesized compounds (1c, 2c, 2d and 3a) have been evaluated for in vitro and antioxidant activity against DPPH radical compared to vitamin C. Compound 2d showed the best DPPH scavenging activity. Compounds 2c, 3a also showed DPPH scavenging activity but less effective than compound 2d. Compound 1c showed DPPH scavenging activity, but effectiveness was very low compared with the previous compounds. Also, compound 2d was evaluated for in vitro cytotoxic activity against human breast cancer (MCF-7) cell line. This compound exhibited the most potent cytotoxic activity at (400 mg/mL) with IC50 value of 96.37 μg/mL

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