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ORIGINAL ARTICLE

# Design, synthesis and biological evaluation of quinazolin-4(3*H*)-one Schiff base conjugates as potential antiamoebic agents

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**Abstract** In an effort to develop novel antiamoebic scaffolds having better efficacy than the standard drug metronidazole ($IC_{50}$ = 1.80 μM) used against *Entamoeba histolytica*, quinazolin-4(3*H*)-one Schiff base conjugates were synthesized and evaluated against HM1: IMSS strain of *E. histolytica*. Out of the thirteen compounds (**S2-S14**), six compounds (**S2**, **S3**, **S4**, **S5**, **S6** and **S11**) were found to be better inhibitors than metronidazole and showed low cytotoxicity on HeLa cells, a cervical cancer cell line. The structure of intermediate compound **S1** was confirmed by crystal structure studies.



## 1. Introduction

Amebiasis, caused by gastrointestinal protozoan *Entamoeba histolytica* is the third principal cause of death among parasitic diseases worldwide. Its prevalence is greatest in the countries with poor sanitation, poverty, ignorance, and malnutrition [1–3]. It is estimated to result in 110,000 deaths and more than 500 million people get infected annually [4]. *E. histolytica* is primarily found in the colon as inactive, but after certain period it becomes lethal to human being by causing severe complications like dysentery, colitis and liver abscess [5–7]. Amoebic colitis characterized by ulceration and inflammation of the colon and amoebic liver abscesses are the two major clinical features of *E. histolytica* infection. Amoebic colitis when accompanied with extreme gut inflammation can closely mimic inflammatory bowel disease [8,9]. Therefore it is important to identify and treat amebiasis appropriately. Although the availability of a large number of antibacterial agents for clinical treatment has proved propitious for the health status of mankind [10]. The existence of antimicrobial resistance for the past few years has threatened their therapeutic utility thereby, exhibiting severe global crisis [11–14]. The antiamoebic drug

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metronidazole is the treatment of choice for this disease but certain side effects [15–18] such as neurologic toxicity [19], genotoxicity, carcinogenicity [18,20,21] spermatozoid damage [22] are associated with it. Moreover resistance of *E. histolytica* to metronidazole and recurrence of intestinal and hepatic amebiasis have been reported [23,24]. This situation has necessitated the development of novel anti-amoebic agents with increased efficacy and lesser toxicity for the host [25]. Because of their high therapeutic index and clinical utility, quinazolin-4(3*H*)-one and its derivatives are promising scaffolds for the synthesis of potential bioactive agents [26]. Quinazolin-4-(3*H*)-ones and 1,2,4-triazoles exhibited a diverse range of bioactivities such as analgesic [27,28], anti-inflammatory [29,30], anti-tumour [31,32], anticancer [33–35], antibacterial [36–38] and anticonvulsant [39–41] therefore, these two important heterocyclic scaffolds have been incorporated into a wide variety of interesting molecules to transform them into better drugs. Due to the important and versatile biological activities, Schiff bases [42] can be used as ideal lead structures in drug development. Therefore, we synthesized quinazolin-4(3*H*)-one Schiff base conjugates with the aim to develop compounds with enhanced antiamoebic efficacy than the standard drug metronidazole [25]. To the best of our knowledge, this is the first report of quinazolin-4-(3*H*)-one derivatives showing promising antiamoebic activity against *E. histolytica*.

## 2. Experimental

### 2.1. Materials and measurements

All the required chemicals were purchased from Merck and Aldrich Chemical Company (USA). Precoated aluminium sheets (Silica gel 60 F254, Merck Germany) were used for thin-layer chromatography (TLC) and spots were visualized under UV light. The melting points were recorded on Veego instrument with model specifications REC-22038 A2 and are uncorrected. Elemental analyses were performed on Elementar Vario analyser and the results are within ±0.4% of the theoretical values. IR spectra (KBr) were acquired at Bruker FT-IR spectrophotometer. $^{1}$H and $^{13}$C NMR were recorded on a Bruker Spectrospin DPX 400 MHz and Bruker Spectrospin DPX 75 MHz spectrometer respectively, using DMSO-$d_6$ as a solvent and trimethylsilane (TMS) as the internal standard. Splitting patterns are designated as follows; s, singlet; d, doublet; t, triplet; m, multiplet. Chemical shift values are given in ppm. Mass spectra were recorded by ESI-MS (AB-Sciex 2000, Applied Biosystem).

### 2.2. General procedure for the synthesis of methyl 2-(2-chloroacetamido)benzoate (*S*)

An aromatic amine (0.12 mol) was dissolved in glacial acetic acid and saturated solution of sodium acetate. The mixture was warmed and then cooled in ice bath with stirring. To this solution was added drop wise a solution of chloro acetyl chloride (0.12 mol). The progress of the reaction was monitored by thin layer chromatography. After half an hour white product was formed. This was separated, filtered, washed with cold water and purified by crystallization from aqueous alcohol [43].

White solid; Yield: 90%; mp: 118 °C; Anal. Calc. (%) for $C_{10}H_{10}ClNO_3$: C, 52.76; H, 4.43; Cl, 15.57; N, 6.15; O, 21.08; found: C, 52.78; H, 4.41; Cl, 15.59; N, 6.14; O, 21.07; $^{1}$H NMR (DMSO-$d_6$) $\delta$ (ppm): 11.31 (s, 1H, NH), 8.39 (d, 1H, $J$ = 8.4 Hz, Ar-H), 7.99 (d, 1H, $J$ = 8.4 Hz, Ar-H), 7.67–7.63 (m, 1H, Ar-H), 7.27 (t, 1H, $J$ = 7.5 Hz, Ar-H), 4.44 (s, 2H, $CH_2$), 3.90 (s, 3H, $OCH_3$); ESI-MS: $m/z$ = 229 ($M^+ + 1$).

### 2.3. Synthesis of methyl 2-(2-(1H-1,2,4-triazol-1-yl)acetamido) benzoate (*S0*)

Methyl 2-(2-chloroacetamido)benzoate (**S**) (0.1 mol) was treated with (0.1 mol) commercially available 1,2,4 triazole in the presence of (0.05 mol) $K_2CO_3$ in dimethylformamide under reflux for 18 h to afford methyl 2-(2-(1*H*-1,2,4-triazol-1-yl)acet amido)benzoate.

White solid; Yield: 92%; mp: 102 °C; Anal. Calc. (%) for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53; O, 18.44; found: C, 55.39; H, 4.64; N, 21.52; O, 18.43; $^{1}$H NMR (DMSO-$d_6$) $\delta$ (ppm): 10.68 (s, 1H, NH), 8.59 (s, 1H, Ar-H), 8.17 (d, 1H, $J$ = 7.8 Hz, Ar-H), 8.05 (s, 1H, Ar-H), 7.92 (d, 1H, $J$ = 7.8 Hz, Ar-H), 7.64 (t, 1H, $J$ = 7.2 Hz, Ar-H), 7.26 (t, 1H, $J$ = 7.2 Hz, Ar-H), 5.24 (s, 2H, $CH_2$), 3.82 (s, 3H, $OCH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 167.67, 165.71, 152.31, 146.15, 138.98, 134.41, 131.08, 124.52, 122.11, 119.17, 61.72, 52.67; ESI-MS: $m/z$ = 261 ($M^+ + 1$).

### 2.4. Synthesis of 2-((1H-1,2,4-triazol-1-yl)methyl)-3-aminoquinazolin-4(3H)-one (*S1*)

Methyl 2-(2-(1*H*-1,2,4-triazol-1-yl)acetamido)benzoate (**S0**) (0.1 mol) was reacted with hydrazine hydrate (0.3 mol) in ethanol under reflux for 12 h to give 2-((1*H*-1,2,4-triazol-1-yl) methyl)-3-aminoquinazolin-4(3*H*)-one.

Yellow solid; Yield: 92%; mp: 66 °C; Anal. Calc. (%) for $C_{11}H_{10}N_6O$: C, 54.54; H, 4.16; N, 34.69; O, 6.60; found: C, 54.55; H, 4.14; N, 34.68; O, 6.61; FT-IR $\nu_{max}$ ($cm^{-1}$): 3477 ($NH_2$), $^{1}$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.64 (s, 1H, Ar-H), 8.16 (d, 1H, $J$ = 7.8 Hz, Ar-H), 8.03 (s, 1H, Ar-H), 7.80 (t, 1H, $J$ = 6.9 Hz, Ar-H), 7.56 (m, 2H, Ar-H), 5.76 (s, 2H, $CH_2$), 5.69 (s, 2H, $NH_2$), $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 161.00, 153.29, 151.68, 146.54, 146.31, 134.79, 127.62, 127.35, 126.47, 120.70, 50.63; ESI-MS: $m/z$ = 265 ($M^+ + 23$).

### 2.5. Synthesis of Schiff bases derived from 2-((1H-1,2,4-triazol-1-yl)methyl)-3-aminoquinazolin-4(3H)-one (*S2-S14*)

An equimolar mixture of compound **S1** (0.01 mol) and substituted aldehydes (0.01 mol) in absolute ethanol (10 mL) was allowed to reflux for 2–4 h, $H_2SO_4$ (0.5 mL) was added slowly to the reaction mixture and progress of the reaction was monitored through thin layer chromatography. When the reaction was completed, it was allowed to cool to attain room temperature. The solid crystalline product was separated out on standing. The solid product was filtered, dried and crystallized from methanol to give title compounds in good yields.

#### 2.5.1. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(2-chlorobenzylideneamino)quinazolin-4(3H)-one (*S2*)

Yield: 82.5%; mp: 115 °C; Anal. Calc. (%) for $C_{18}H_{13}ClN_6O$: C, 59.27; H, 3.59; Cl, 9.72; N, 23.04; O, 4.39; found: C, 59.25; H, 3.58; Cl, 9.70; N, 23.06; O, 4.37; FT-IR $\nu_{max}$ ($cm^{-1}$): 1687 (C═O), 1610 (C═N); $^{1}$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.51

(s, 1H, CH═N), 8.61 (s, 1H, Ar-H), 8.26–8.20 (m, 2H, Ar-H), 8.01 (s, 1H, Ar-H), 7.87 (t, 1H, $J$ = 7.7 Hz, Ar-H), 7.66–7.62 (m, 2H, Ar-H), 7.60–7.55 (m, 3H, Ar-H), 5.78 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 163.56, 158.30, 151.10, 150.66, 145.87, 145.74, 135.70, 135.35, 134.73, 130.82, 130.20, 128.67, 128.42, 127.92, 127.79, 127.43, 121.85, 51.46; ESI-MS: $m/z$ = 365 ($M^+ + 1$).

### 2.5.2. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(3-chlorobenzylideneamino)quinazolin-4(3H)-one (**S3**)

Yield: 85%; mp: 131 °C; Anal. Calc. (%) for $C_{18}H_{13}ClN_6O$: C, 59.27; H, 3.59; Cl, 9.72; N, 23.04; O, 4.39; found: C, 59.25; H, 3.57; Cl, 9.72; N, 23.08; O, 4.35; FT-IR $\nu_{max}$ ($cm^{-1}$): 1676 (C═O), 1606 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.12 (s, 1H, CH═N), 8.62 (s, 1H, Ar-H), 8.21 (d, 1H, $J$ = 7.8 Hz, Ar-H), 8.06 (s, 1H, Ar-H), 8.01 (s, 1H, Ar-H), 7.93 (d, 1H, $J$ = 7.2 Hz, Ar-H), 7.87 (t, 1H, $J$ = 7.5 Hz, Ar-H), 7.63 (d, 1H, $J$ = 7.8 Hz, Ar-H), 7.60–7.57 (m, 3H, Ar-H), 5.76 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 167.01, 157.98, 151.55, 150.64, 145.95, 145.82, 135.31, 134.90, 134.42, 132.90, 131.49, 128.38, 128.29, 127.91, 127.82, 127.31, 121.72, 51.37; ESI-MS: $m/z$ = 365 ($M^+ + 1$).

### 2.5.3. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(4-chlorobenzylideneamino)quinazolin-4(3H)-one (**S4**)

Yield: 85%; mp: 120 °C; Anal. Calc. (%) for $C_{18}H_{13}ClN_6O$: C, 59.27; H, 3.59; Cl, 9.72; N, 23.04; O, 4.39; found: C, 59.24; H, 3.56; Cl, 9.71; N, 23.07; O, 4.36; FT-IR $\nu_{max}$ ($cm^{-1}$): 1677 (C═O), 1604 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.09 (s, 1H, CH═N), 8.61 (s, 1H, Ar-H), 8.20 (d, 1H, $J$ = 7.5 Hz, Ar-H), 7.44 (d, 3H, $J$ = 7.4 Hz, Ar-H), 7.86 (t, 1H, $J$ = 7.3 Hz, Ar-H), 7.67 (d, 2H, $J$ = 8.4 Hz, Ar-H), 7.61 (t, 2H, $J$ = 8.8 Hz, Ar-H), 5.75 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 167.55, 157.97, 151.32, 150.54, 145.86, 137.98, 135.29, 131.67, 131.03, 129.77, 127.91, 127.82, 127.30, 121.74, 51.42; ESI-MS: $m/z$ = 365 ($M^+ + 1$).

### 2.5.4. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(4-nitrobenzylideneamino)quinazolin-4(3H)-one (**S5**)

Yield: 78%; mp: 109 °C; Anal. Calc. (%) for $C_{18}H_{13}N_7O_3$: C, 57.60; H, 3.49; N, 26.12; O, 12.79; found: C, 57.61; H, 3.48; N, 26.10; O, 12.78; FT-IR $\nu_{max}$ ($cm^{-1}$): 1676 (C═O), 1614 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.36 (s, 1H, CH═N), 8.62 (s, 1H, Ar-H), 8.40 (d, 2H, $J$ = 8.4 Hz, Ar-H), 8.25 (t, 3H, $J$ = 8.7 Hz, Ar-H), 8.00 (s, 1H, Ar-H), 7.85–7.68 (m, 1H, Ar-H), 7.59 (d, 2H, $J$ = 8.1 Hz, Ar-H), 5.80 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm) 165.73, 158.13, 151.88, 150.79, 150.14, 146.07, 145.81, 138.74, 135.53, 130.49, 128.10, 127.93, 127.45, 124.71, 121.80, 51.41; ESI-MS: $m/z$ = 376 ($M^+ + 1$).

### 2.5.5. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(furan-2-ylmethyleneamino)quinazolin-4(3H)-one (**S6**)

Yield: 91%; mp: 194 °C; Anal. Calc. (%) for $C_{16}H_{12}N_6O_2$: C, 60.00; H, 3.78; N, 26.24; O, 9.99; found: C, 60.01; H, 3.79; N, 26.25; O, 9.97; FT-IR $\nu_{max}$ ($cm^{-1}$): 1669 (C═O), 1600 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.89 (s, 1H, CH═N), 8.59 (s, 1H, Ar-H), 8.19 (d, 2H, $J$ = 7.5 Hz, Ar-H), 7.99 (s, 1H, Ar-H), 7.86 (t, 1H, $J$ = 7.5 Hz, Ar-H), 7.61 (t, 2H, $J$ = 7.8 Hz, Ar-H), 7.37 (s, 1H, Ar-H), 6.82 (s, 1H, Ar-H), 5.68 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 158.04, 156.98, 151.82, 150.54, 148.71, 147.88, 146.20, 145.87, 135.16, 127.78, 127.24, 121.73, 121.13, 113.51, 51.22; ESI-MS: $m/z$ = 321 ($M^+ + 1$).

### 2.5.6. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(2,5-dimethoxybenzylideneamino)quinazolin-4(3H)-one (**S7**)

Yield: 91%; mp: 194 °C; Anal. Calc. (%) for $C_{20}H_{18}N_6O_3$: C, 61.53; H, 4.65; N, 21.53; O, 12.29; found: C, 61.51; H, 4.62; N, 21.52; O, 12.28; FT-IR $\nu_{max}$ ($cm^{-1}$): 1682 (C═O), 1606 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.21 (s, 1H, CH═N), 8.63 (s, 1H, Ar-H), 8.20 (d, 1H, $J$ = 7.2 Hz, Ar-H), 8.03 (s, 1H, Ar-H), 7.85 (t, 1H, $J$ = 7.8 Hz, Ar-H), 7.60–7.43 (m, 3H, Ar-H), 7.24–7.21 (m, 1H, Ar-H), 7.17 (d, 1H, $J$ = 9.0 Hz, Ar-H), 5.68 (s, 2H, $CH_2$), 3.83 (s, 3H, $OCH_3$), 3.81 (s, 3H, $OCH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 163.65, 158.12, 154.44, 153.71, 151.01, 150.49, 145.89, 135.13, 127.77, 127.31, 121.87, 121.79, 120.90, 114.30, 110.27, 56.88, 56.12, 51.61; ESI-MS: $m/z$ = 391 ($M^+ + 1$).

### 2.5.7. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(4-methoxybenzylideneamino)quinazolin-4(3H)-one (**S8**)

Yield: 88%; mp: 125 °C; Anal. Calc. (%) for $C_{19}H_{16}N_6O_2$: C, 63.32; H, 4.48; N, 23.32; O, 8.88; found: C, 63.31; H, 4.49; N, 23.31; O, 8.89; FT-IR $\nu_{max}$ ($cm^{-1}$): 1674 (C═O), 1599 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.27 (s, 1H, CH═N), 8.31 (s, 1H, Ar-H), 8.21 (d, 1H, $J$ = 7.8 Hz, Ar-H), 8.07 (d, 2H, $J$ = 8.4 Hz, Ar-H), 7.83 (t, 1H, $J$ = 7.5 Hz, Ar-H), 7.70 (d, 2H, $J$ = 8.2 Hz, Ar-H), 7.60 (t, 2H, $J$ = 7.5 Hz, Ar-H), 7.52 (d, 1H, $J$ = 8.0 Hz, Ar-H), 5.63 (s, 2H, $CH_2$), 3.32 (s, 3H, $OCH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$: 168.94, 163.47, 158.00, 151.74, 150.57, 146.00, 135.07, 131.41, 127.77, 127.19, 125.14, 121.79, 115.08, 56.04, 51.29; ESI-MS: $m/z$ = 361 ($M^+ + 1$).

### 2.5.8. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(benzylideneamino)quinazolin-4(3H)-one (**S9**)

Yield: 82%; mp: 110 °C; Anal. Calc. (%) for $C_{18}H_{14}N_6O$: C, 65.44; H, 4.27; N, 25.44; O, 4.84; found: C, 65.42; H, 4.25; N, 25.46; O, 4.85; FT-IR $\nu_{max}$ ($cm^{-1}$): 1682 (C═O), 1612 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.03 (s, 1H, CH═N), 8.59 (s, 1H, Ar-H), 8.21 (d, 1H, $J$ = 7.5 Hz, Ar-H), 7.99 (s, 1H, Ar-H), 7.95 (d, 2H, $J$ = 7.2 Hz, Ar-H), 7.87 (t, 1H, $J$ = 7.7 Hz, Ar-H), 7.65–7.58 (m, 5H, Ar-H), 5.74 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 169.16, 157.97, 151.84, 150.61, 146.04, 145.95, 135.21, 133.34, 132.72, 129.60, 129.40, 127.83, 127.28, 121.79, 51.27; ESI-MS: $m/z$ = 331 ($M^+ + 1$).

### 2.5.9. (E)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-((1H-indol-3-yl)methyleneamino)quinazolin-4(3H)-one (**S10**)

Yield: 87%; mp: 151 °C; Anal. Calc. (%) for $C_{20}H_{15}N_7O$: C, 65.03; H, 4.09; N, 26.54; O, 4.33; found: C, 65.01; H, 4.08; N, 26.53; O, 4.32; FT-IR $\nu_{max}$ ($cm^{-1}$): 1667 (C═O), 1603 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 12.08 (s, 1H, NH) 8.91 (s, 1H, CH═N), 8.75 (s, 1H, Ar-H), 8.26–8.12 (m, 4H, Ar-H), 7.85 (t, 1H, $J$ = 7.5 Hz, Ar-H), 7.60 (t, 3H, $J$ = 8.4 Hz, Ar-H), 7.33–7.25 (m, 2H, Ar-H), 5.81 (s, 2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 165.85, 158.26, 150.94, 150.63, 146.11, 145.89, 137.88, 136.31, 134.80, 127.71,

127.51, 127.08, 124.69, 123.79, 122.59, 122.16, 121.93, 112.87, 110.68, 51.39; ESI-MS: $m/z$ = 370 ($M^+ + 1$).

#### 2.5.10. (*E*)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-((3-methylthiophen-2-yl)methyleneamino)quinazolin-4(3H)-one (*S11*)

Yield: 91%; mp: 194 °C; Anal. Calc. (%) for $C_{17}H_{14}N_6OS$: C, 58.27; H, 4.03; N, 23.98; O, 4.57; S, 9.15; found: C, 58.25; H, 4.01; N, 23.99; O, 4.56; S, 9.16; FT-IR $\nu_{max}$ ($cm^{-1}$): 1671 (C═O), 1599 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 9.17 (s, 1H, CH═N), 8.65 (s, 1H, Ar-H), 8.20 (d, 1H, $J$ = 7.5 Hz, Ar-H), 8.06 (s, 1H, Ar-H), 7.91–7.75 (m, 2H, Ar-H), 7.61–7.55 (m, 2H, Ar-H), 7.13–7.11 (m, 1H, Ar-H), 5.66 (s, 2H, $CH_2$), 2.27 (s, 3H, $CH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 162.97, 158.07, 151.38, 150.25, 146.63, 145.96, 135.07, 132.96, 131.96, 130.56, 127.76, 127.71, 127.25, 121.76, 51.24, 14.37; ESI-MS: $m/z$ = 351 ($M^+ + 1$).

#### 2.5.11. (*E*)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(2-methylbenzylideneamino)quinazolin-4(3H)-one (*S12*)

Yield: 85%; mp: 119 °C; Anal. Calc. (%) for $C_{19}H_{16}N_6O$: C, 66.27; H, 4.68; N, 24.40; O, 4.65; found: C, 66.28; H, 4.69; N, 24.41; O, 4.62; FT-IR $\nu_{max}$ ($cm^{-1}$): 1681 (C═O), 1605 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.94 (s, 1H, CH═N), 8.58 (s, 1H, Ar-H), 8.20 (d, 1H, $J$ = 7.2 Hz, Ar-H), 7.98 (s, 1H, Ar-H), 7.85 (d, 3H, $J$ = 6.9 Hz, Ar-H), 7.61–7.56 (m, 2H, Ar-H), 7.40 (d, 2H, $J$ = 7.2 Hz, Ar-H), 5.74 (s, 2H, $CH_2$), 2.50 (s, 3H, $CH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 169.13, 157.99, 151.82, 150.58, 146.01, 145.98, 143.71, 135.15, 130.19, 130.04, 129.41, 127.80, 127.46, 127.25, 123.64, 121.81, 117.72, 51.30, 21.77; ESI-MS: $m/z$ = 345 ($M^+ + 1$).

#### 2.5.12. (*E*)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(4-(dimethylamino)benzylideneamino)quinazolin-4(3H)-one (*S13*)

Yield: 81%; mp: 210 °C; Anal. Calc. (%) for $C_{20}H_{19}N_7O$: C, 64.33; H, 5.13; N, 26.26; O, 4.28; found: C, 64.31; H, 5.12; N, 26.25; O, 4.27; FT-IR $\nu_{max}$ ($cm^{-1}$): 1672 (C═O), 1597 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.62 (s, 1H, CH═N), 8.56 (s, 1H, Ar-H), 8.17 (d, 1H, $J$ = 7.8 Hz, Ar-H), 7.97 (s, 1H, Ar-H), 7.81–7.71 (m, 3H, Ar-H), 7.59–7.54 (m, 2H, Ar-H), 6.83 (d, 2H, $J$ = 8.7 Hz, Ar-H), 5.66 (s, 2H, $CH_2$), 3.04 (s, 6H, $2CH_3$); $^{13}$C NMR (DMSO-$d_6$) $\delta$ (ppm): 169.48, 158.15, 153.73, 151.78, 150.67, 146.02, 134.86, 131.15, 127.74, 127.57, 127.10, 121.84, 119.26, 111.96, 51.27, 39.79; ESI-MS: $m/z$ = 374 ($M^+ + 1$).

#### 2.5.13. (*E*)-2-((1H-1,2,4-Triazol-1-yl)methyl)-3-(benzo[d][1,3]dioxol-5-ylmethyleneamino)quinazolin-4(3H)-one (*S14*)

Yield: 91%; mp: 110 °C; Anal. Calc. (%) for $C_{19}H_{14}N_6O_3$: C, 60.96; H, 3.77; N, 22.45; O, 12.82; found: C, 60.94; H, 3.75; N, 22.48; O, 12.81; FT-IR $\nu_{max}$ ($cm^{-1}$): 1667 (C═O), 1608 (C═N); $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.86 (s, 1H, CH═N), 8.60 (s, 1H, Ar-H), 8.18 (d, 1H, $J$ = 8.1 Hz, Ar-H), 7.98 (s, 1H, Ar-H), 7.85–7.80 (t, 1H, $J$ = 7.5 Hz, Ar-H), 7.60–7.52 (m, 3H, Ar-H), 7.40 (d, 1H, $J$ = 8.1 Hz, Ar-H), 7.10 (d, 1H, $J$ = 8.1 Hz, Ar-H), 6.17 (s, 2H, Ar-H), 5.72 (s, 2H, $CH_2$); $^{13}$C NMR(DMSO-$d_6$) $\delta$ (ppm): 168.38, 158.01, 151.90, 151.66, 150.60, 148.71, 145.94, 135.11, 127.77, 127.65, 127.21, 126.97, 121.76, 109.05, 106.31, 102.57, 51.37; ESI-MS: $m/z$ = 375 ($M^+ + 1$).

### 2.6. X-ray crystal structure determination

Three-dimensional X-ray data were collected on a Bruker Kappa Apex CCD diffractometer at low temperature for **S1** by the $\phi$–$\omega$ scan method. Reflections were measured from a hemisphere of data collected from frames, each of them covering 0.3° in $\omega$. 13,269 reflections measured were corrected for Lorentz and polarization effects and for absorption by multi-scan methods based on symmetry-equivalent and repeated reflections. Of them, 1834 independent reflections exceeded the significance level ($|F|/\sigma|F|$) > 4.0. After data collection, in each case a multi-scan absorption correction (SADABS) [44] was applied, and the structure was solved by direct methods and refined by full matrix least-squares on $F^2$ data using SHELX suite of programs [45]. Hydrogen atoms were located in difference Fourier map and left to refine freely. Refinements were done with allowance for thermal anisotropy of all non-hydrogen atoms. A final difference Fourier map showed no residual density in the crystal 0.243 and −0.384 e.Å$^{-3}$. A weighting scheme $w = 1/[\sigma^2(F_o^2) + (0.086100\ P)^2 + 0.064000\ P]$, was used in the latter stages of refinement. Further details of the crystal structure determination are given in Tables 1 and 2. CCDC 1416608 contains the supplementary crystallographic data for the structure **S1** reported in this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk.

### 2.7. In vitro antiamoebic assay

The synthesized compounds were screened against the HM1: IMSS strain of *E. histolytica* using microdilution method

**Table 1** Crystal data and structure refinement for the compound 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**).

| | **S1** |
|---|---|
| Formula | $C_{11}H_{10}N_6O$ |
| Formula weight | 242.25 |
| T (*K*) | 100(2) |
| Wavelength (Å) | 0.71073 |
| Crystal system | Monoclinic |
| Space group | $P2_1/c$ |
| *a* (Å) | 4.63170(10) |
| *b* (Å) | 18.4777(5) |
| *c* (Å) | 12.4608(4) |
| $\beta$ (°) | 98.441(2) |
| *V* (Å$^3$) | 1054.88(5) |
| *Z* | 4 |
| $F_{000}$ | 504 |
| $D_{calc}$ (g cm$^{-3}$) | 1.525 |
| $\mu$ (mm$^{-1}$) | 0.107 |
| $\theta$ (°) | 1.99–26.38 |
| $R_{int}$ | 0.0300 |
| Crystal size (mm$^3$) | 0.50 × 0.41 × 0.30 |
| Goodness-of-fit on $F^2$ | 1.161 |
| $R_1[I > 2\sigma(I)]$[a] | 0.0351 |
| $wR_2$ (all data)[b] | 0.1310 |

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.
[b] $wR_2 = \{\Sigma[w(||F_o|^2 - |F_c|^2|)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

**Table 2** Bond lengths [Å] and angles [°] for the compound 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**).

| Bond lengths | S1 |
|---|---|
| O(1)–C(5) | 1.2267(17) |
| N(1)–C(2) | 1.319(2) |
| N(1)–C(1) | 1.350(2) |
| C(1)–N(2) | 1.320(2) |
| N(2)–N(3) | 1.3578(17) |
| C(2)–N(3) | 1.330(2) |
| N(3)–C(3) | 1.4452(17) |
| N(4)–N(6) | 1.4128(16) |
| C(4)–N(5) | 1.2879(18) |
| C(4)–N(6) | 1.3775(17) |
| N(5)–C(11) | 1.3931(18) |
| C(5)–N(6) | 1.3943(19) |
| **Angles** | **S1** |
| C(2)–N(1)–C(1) | 102.34(13) |
| N(2)–C(1)–N(1) | 115.42(14) |
| C(1)–N(2)–N(3) | 101.72(12) |
| N(1)–C(2)–N(3) | 110.64(14) |
| C(2)–N(3)–N(2) | 109.88(12) |
| C(2)–N(3)–C(3) | 128.61(12) |
| N(2)–N(3)–C(3) | 121.51(12) |
| N(5)–C(4)–N(6) | 123.95(13) |
| C(4)–N(5)–C(11) | 117.08(12) |

[46]. All the experiments were carried out in triplicate at each concentration level and repeated thrice. *E. histolytica* trophozoites were cultured in the TYI-S-33 growth medium in wells of 96-well microtiter plates [47]. DMSO (40 µL) was added to all the samples (1 mg) followed by enough culture medium to obtain concentration of 1 mg/mL. The maximum concentration of DMSO in the test did not exceed 0.1%, and at this level no inhibition of amoebal growth had occurred. Compounds were further diluted with medium to a concentration of 0.1 mg/mL. Two fold serial dilutions were made in the wells of 96-well microtiter plate. Each test included metronidazole (MNZ) as the standard amoebicidal drug, control (culture medium plus parasite) and a blank (culture medium only). The cell suspension was then diluted to $10^5$ organism/mL by adding fresh medium and 170 µL of this suspension was added to the test and control well in the plate. Plate was sealed and gassed for 10 min with nitrogen before incubation at 37 °C for 72 h. After incubation, the growth of amoebae in the plate was checked with a low power microscope and the optical density of the solution in each well was determined at 490 nm with a microplate reader. The % inhibition of amoebal growth was calculated from the optical densities of the control and test wells and plotted against the logarithm of the dose of the drug tested. Linear regression analysis was used to determine the best-fitted straight line from which the $IC_{50}$ value was found.

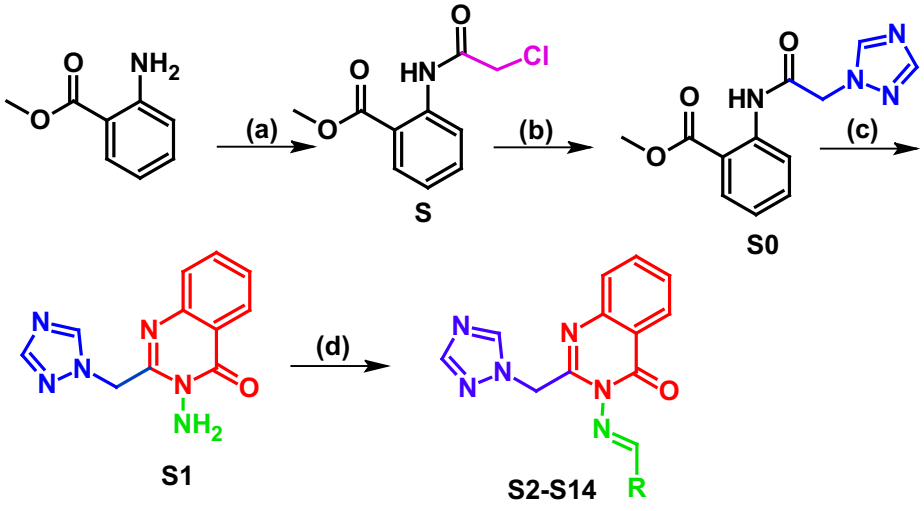
### 2.8. MTT assay

Cytotoxicity of the drugs was checked using MTT assay [48]. This is a colorimetric assay that measures the reduction of yellow 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) by mitochondrial succinate dehydrogenase. The MTT enters the cells and passes into the mitochondria where it is reduced to an insoluble, coloured (dark purple) formazan product. Since reduction of MTT can only occur in metabolically active cells, the level of activity is a measure of the viability of the cells. This formazan product is then dissolved using organic solvents such as DMSO and absorbance was taken using spectrophotometer. To assess the effect of the compounds, HeLa cells (4000 cells/well), were plated in 96 well tissue culture plates in triplicate. Each of the compounds was added at their $IC_{50}$ concentrations, as seen in *E. histolytica*, as shown in Fig. 5. The cells were incubated for different time lengths (48 h and 72 h) and cell viability assay was performed after completion of the stipulated time intervals.

## 3. Results and discussion

### 3.1. Chemistry

All the target compounds (**S2**–**S14**) were synthesized in a four step reaction procedure as outlined in Scheme 1. The methyl




**Scheme 1** Synthesis of quinazolin-4(3*H*)-one Schiff base conjugates. Reagents and conditions: (a) $ClCH_2COCl$, AcOH, sat. NaOAc solution, rt. (b) 1,2,4-Triazole, DMF, $K_2CO_3$, reflux. (c) $N_2H_4{\cdot}xH_2O$, EtOH, reflux. (d) RCHO, EtOH, $H_2SO_4$, reflux.

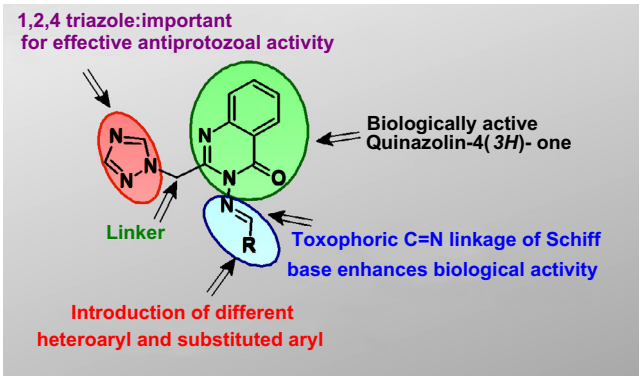



**Figure 1** Designing of hybrid molecule.

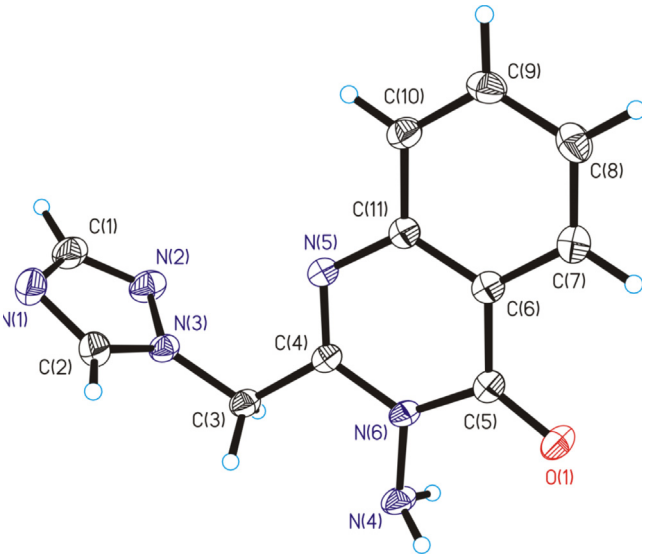



**Figure 2** ORTEP plot of the compound 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**). All the non-hydrogen atoms are presented by their 50% probability ellipsoids. Hydrogen atoms are omitted for clarity.

2-(2-chloroacetamido)benzoate (**S**) was synthesized from methyl anthranilate according to the procedure described in the literature [43]. Compound **S** was further reacted with commercially available 1,2,4 triazole by nucleophilic

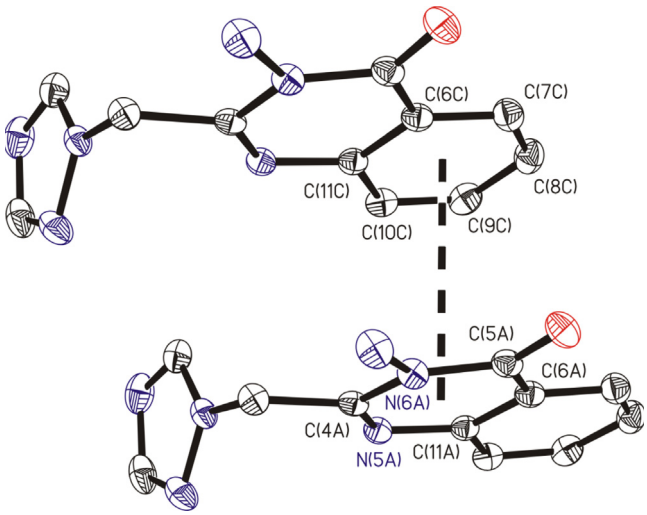



**Figure 4** π–π stacking interactions determine the management of molecules in the crystal packing.

substitution reaction in the presence of dimethylformamide and $K_2CO_3$ to afford methyl 2-[(1*H*-1,2,4-triazol-1-ylacetyl) amino]benzoate (**S0**) which reacted with hydrazine hydrate in ethanol to give 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**). Further, the condensation reaction of intermediate (**S1**) with various aldehydes furnished the final compounds in good yields (**S2**–**S14**). The compounds are stable in solid states at room temperature. All the synthesized compounds gave satisfactory spectral data for the proposed structures. Characteristic IR spectra showed a significant band for the formation of compound **S1** where the appearance of strong absorptions at 3477 $cm^{-1}$ was assigned to the presence of –NH. The absence of –NH stretching and presence of C═N stretching in the IR spectra of compounds (**S2**–**S14**) at 1597–1614 $cm^{-1}$ established the conversion of –NH into its Schiff base. The proposed structures were further confirmed by recording the proton NMR. In the $^1$H NMR spectra of compounds (**S2**–**S14**), N═CH proton resonated as a singlet at $\delta$ 8.62–9.51 ppm. The signals due to the aromatic protons appeared in the expected region. The configuration (*E* or *Z* form) of the target compounds was confirmed by 2D-NOESY $^1$H NMR spectroscopy. Based on the analysis of our 2D NOESY NMR, we have concluded that Schiff bases

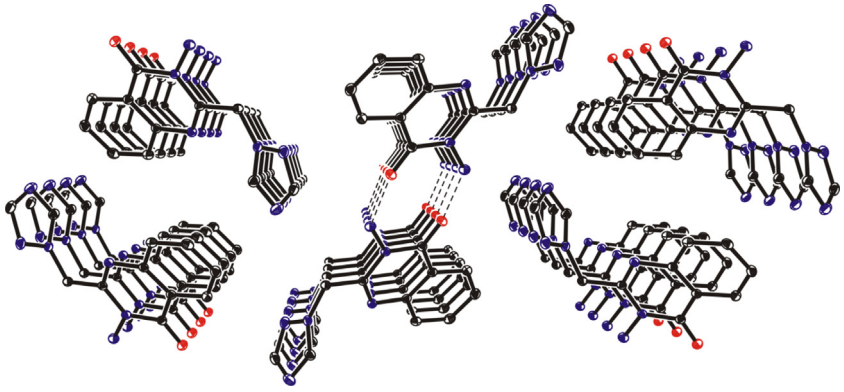
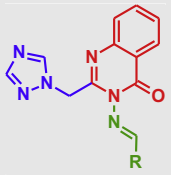
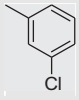
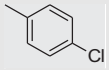
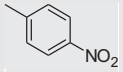
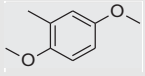
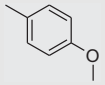
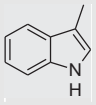
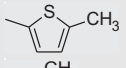
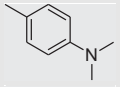
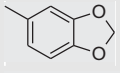
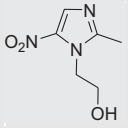


**Figure 3** Crystal packing of the compound 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**). Hydrogen bonds are present in dashed black lines.

**Table 3** *In vitro* antiamoebic activity of quinazolin-4(3*H*)-one Schiff base conjugates (**S2**–**S14**) against HM1: IMSS strain of *E. histolytica* and measurement of cell viability by MTT assay.



| Compound code | R | Antiamoebic activity ($IC_{50}$ ± S.D.) | Cytotoxicity ($IC_{50}$ ± S.D.) | |
|---|---|---|---|---|
| | | | 48 h | 72 h |
| **S0** | – | 2.85 ± 0.01 | N.D | N.D |
| **S1** | – | 1.47 ± 0.03 | 87.46 ± 7.11 | 90.23 ± 0.83 |
| **S2** |  | 1.10 ± 0.01 | 89.76 ± 3.05 | 92.86 ± 3.21 |
| **S3** |  | 0.72 ± 0.05 | 91.60 ± 1.31 | 86.43 ± 1.40 |
| **S4** |  | 1.41 ± 0.02 | 84.96 ± 3.95 | 91.96 ± 2.89 |
| **S5** |  | 0.82 ± 0.02 | 85.33 ± 4.06 | 90.46 ± 3.03 |
| **S6** |  | 0.96 ± 0.08 | 82.46 ± 3.35 | 93.8 ± 2.32 |
| **S7** |  | 5.01 ± 0.05 | N.D | N.D |
| **S8** |  | 4.39 ± 0.02 | N.D | N.D |
| **S9** |  | 4.12 ± 0.04 | N.D | N.D |
| **S10** |  | 5.19 ± 0.02 | N.D | N.D |
| **S11** |  | 0.97 ± 0.06 | 89.20 ± 5.89 | 97.46 ± 1.11 |
| **S12** |  | 4.98 ± 0.04 | N.D | N.D |
| **S13** |  | 5.32 ± 0.01 | N.D | N.D |
| **S14** |  | 6.87 ± 0.03 | N.D | N.D |
| MNZ |  | 1.80 ± 0.01 | 96.13 ± 1.40 | 96.03 ± 1.55 |

(**S2**–**S14**) exist in *E* configuration in DMSO solution. Also according to the literature the compounds containing imine bond are present in higher percentage in dimethyl $D_6$ Sulfoxide solution in the form of geometrical *E*-isomer about ─C═N double bond [49]. The structure of all the compounds was further elucidated by mass spectral studies. All the compounds produced C, H, and N values within 0.4% from the theoretical values, which was acceptable.

### 3.2. Single crystal structure of compound **S1**

ORTEP diagram for the compound 3-amino-2-(1*H*-1,2,4-triazol-1-ylmethyl)quinazolin-4(3*H*)-one (**S1**) is shown in Fig. 2. Selected bond distances and angles are given in Table 2. Atoms C1, C2 and C3 are coplanar with the nitrogen atoms N1, N2 and N3 of triazole ring, mean deviation from the least-squares plane being 0.0027(10) Å. The interatomic distances within the triazole ring are not equal, ranging from 1.319(2) to 1.350(2) Å, and agree with the values observed in the literature [50]. The N2–C1 bond length, 1.320(2) Å, N3–C2 bond length, 1.330(2) Å and N1–C2 bond length, 1.319(2) Å, are significantly shorter than the N1–C1, which is 1.350(2) Å and these are longer than the average value of the lengths of the double bonds in related triazole thiones [1.300(2) Å; Cambridge. Structural Database, version 5.26; ConQuest, version 3.6] [50]. This is attributed to the presence of a non uniform delocalization between the lone pair on nitrogen atoms and the next atoms in the triazole ring. The N3–C3 bond length is 1.4452(17) Å similar to other N–C bonds in triazole substituted rings [51]. The presence of intermolecular forces between the rings of quinazoline group determines the crystal packing. Intermolecular hydrogen bonds between the amine group and oxo group of two different quinazoline groups determine the structure of the compound. π–π stacking interactions between the rings establish the link between frameworks and determine the structure in layers. The distances between π clouds of the centroids in the rings of quinazoline groups are: $d_{c1–c2}$ = 3.641 Å [c1 (C4A–C5A–C6A–C11A–N5A–N6A) and c2 (C6C–C7C–C8C–C9C–C10C–C11C)] and repeated for other centroids (Figs. 3 and 4).

### 3.3. Evaluation of biological activities

#### 3.3.1. Antiamoebic activity

To scrutinize the antiamoebic potential of the synthesized compounds (**S1**–**S14**), they were screened against HM1: IMSS strain of *E. histolytica* using metronidazole as reference amoebicidal drug which had a 50% inhibitory concentration ($IC_{50}$) 1.80 μM in our experiments. All the experiments were carried out in triplicate at each concentration level and repeated thrice. Cytotoxicity of the compounds having $IC_{50}$ value less than metronidazole was assessed by MTT assay on human cervical cancer HeLa cell line. The results of antiamoebic activity and cytotoxicity are summarized in Table 3. Antiamoebic results suggest that the intermediate compound **S1** ($IC_{50}$ = 1.47 μM) incorporating both quinazolin-4(3*H*)-one and 1,2,4-triazole ring was a more potent amoebicidal agent than **S0** ($IC_{50}$ = 2.85 μM) incorporating only 1,2,4-triazole. Furthermore compound **S1** had lower $IC_{50}$ values than MNZ. We further synthesized Schiff base conjugates. All the final compounds have $IC_{50}$ values in the range 0.72–6.87 μM. Out of the thirteen synthesized compounds, six compounds: **S2** ($IC_{50}$ = 1.10 μM), **S3** ($IC_{50}$ = 0.72 μM), **S4** ($IC_{50}$ = 1.41 μM), **S5** ($IC_{50}$ = 0.82 μM), **S6** ($IC_{50}$ = 0.96 μM) and **S11** ($IC_{50}$ = 0.97 μM) were found to exhibit better antiamoebic activity than intermediate compound **S1** and the standard drug MNZ ($IC_{50}$ = 1.80 μM). Compound **S3** having weak deactivating chloro group at *meta* position of phenyl ring, exhibited promising activity ($IC_{50}$ = 0.72 μM) than compounds **S4** ($IC_{50}$ = 1.41 μM) and **S2** ($IC_{50}$ = 1.10 μM), where the chloro group is present at *para* and *ortho* positions respectively. Introduction of strong deactivating nitro group **S5** ($IC_{50}$ = 0.82 μM), at *para* position of phenyl ring exerts significant inhibitory activity, whereas the presence of strong activating methoxy group **S8** ($IC_{50}$ = 4.39 μM), and N,N dimethylamine **S13** ($IC_{50}$ = 5.32 μM) group at the same position exhibited less activity. Weak activating methyl group which increases the electron density through hyperconjugation to the aromatic ring, when present at *ortho* position, **S12** ($IC_{50}$ = 4.98 μM) showed less activity than the unsubstituted phenyl ring, **S9** ($IC_{50}$ = 4.12 μM). However, the activity decreased in compound **S7** by inserting two methoxy groups at positions 2 and 5 of the phenyl ring ($IC_{50}$ = 5.01 μM). The study of structure activity relationships of the synthesized compounds indicate that the replacement of substituted phenyl ring of Schiff base with bulky piperonal **S14** ($IC_{50}$ = 6.87 μM) and indole ring **S10** ($IC_{50}$ = 5.19 μM) resulted in the dramatic decrease in the activity due to the reduced aromaticity or the bulky nature of the group which might be imposing steric hindrance. However, the presence of heteroaromatic ring like thiophene **S11** ($IC_{50}$ = 0.97 μM) and furan **S6** ($IC_{50}$ = 0.96 μM) was helpful in increasing the activity of the compounds. Thus from the above discussion it can be concluded that compound **S3** seems to be the most potent of all the compounds screened.

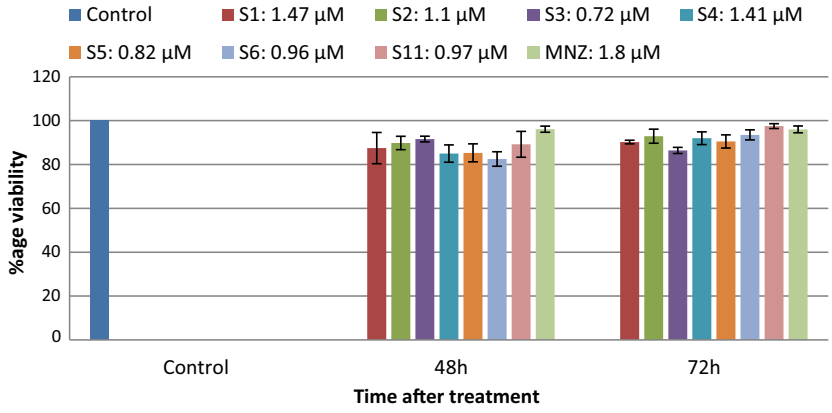



**Figure 5** Assessment of viability of HeLa cells in response to compounds **S1**, **S2**, **S3**, **S4**, **S5**, **S6** and **S11** at their $IC_{50}$. Cells were plated in triplicate for 48 h and 72 h and treated with the compounds. Cells treated with DMSO are used as the control. MTT was added after completion of stipulated time intervals and processed. Absorbance was taken at 570 nm.

*3.3.2. Cytotoxicity*

To assess the effect of the compounds on cervical cancer cell line, HeLa cells (4000 cells/well), were plated in 96 well tissue culture plates in triplicate. Each of the compounds was added at the concentrations of their $IC_{50}$ as seen in *E. histolytica*, as shown in Fig. 5. The cells were incubated for different time lengths (48 h and 72 h) and cell viability assay was performed after completion of the stipulated time intervals. As seen in Table 3, when cells were treated with compounds **S1**, **S2**, **S4**, **S5**, **S6** and **S11** at their $IC_{50}$, more than 90% cell viability was observed while **S3** resulted in cell viability of 86.4%. Thus above results showed that there is no significant reduction in cell viability of HeLa cells on treatment with the above mentioned compounds.

## 4. Conclusion

To conclude, this paper describes the synthesis and biological evaluation of quinazolin-4(3*H*)-one Schiff base conjugates as inhibitors of *E. histolytica*. The *in vitro* study suggested that some quinazolin-4(3*H*)-one derivatives exhibited potent amoebicidal activity than the standard drug. It was also observed that the intermediate compound **S1** incorporating both quinazolin-4(3*H*)-one and 1,2,4-triazole ring displayed better activity ($IC_{50}$ = 1.47 μM) than **S0**. Therefore, we hypothesized that the combination of two biologically important heterocyclic scaffolds, quinazolin-4(3*H*)-one and 1,2,4-triazole in **S1**, is expected to exhibit synergistic effects to display antiamoebic activity. As the basic skeleton of compound **S1** ($IC_{50}$ = 1.47 μM) is entirely different from **S0** ($IC_{50}$ = 2.85 μM), it can be concluded that the entire molecular-skeleton of the particular compound is concerned with its $IC_{50}$ value and therefore, responsible for its antiamoebic activity. The structure activity relationship (SAR), of the compounds (**S2**–**S14**) shared three common features: the presence of 1,2,4-triazole ring, azomethine linkage and quinazolin-4(3*H*)-one ring (Fig. 1) but differ in their corresponding antiamoebic activity. It may be due to the different substituents on the phenyl ring of Schiff bases. The presence of heteroaromatic rings like furan and thiophene, electron withdrawing groups like nitro group on *meta* position and weakly deactivating group like chloro on *ortho*, *meta* and *para* position of the phenyl ring of Schiff bases generally increase the antiamoebic activity. Also, the entire molecular-skeleton of the particular compound is responsible for its antiamoebic activity. Out of all the screened compounds only seven compounds (**S1**, **S2**, **S3**, **S4**, **S5**, **S6** and **S11**) were found to be better inhibitors of growth *E. histolytica* than the reference drug metronidazole. MTT assay revealed that there is no significant reduction in cell viability of HeLa cells on treatment with the above mentioned compounds at their $IC_{50}$. Thus these compounds show low cytotoxicity. In the present work we have adopted simple synthetic strategy to design target motifs which will encourage further advancement in the synthesis of novel derivatives to conduct comprehensive evaluation of their biological activities.

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