Mohammad Mumtaz Alam et al. / Journal of Pharmacy Research 2014,8(1),77-80

Research Article
ISSN: 0974-6943

Available online through
http://jprsolutions.info

Synthesis and *in-vitro* antimalarial evaluation of Pyrazoline: A new antimalarial Scaffold

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Received on:21-11-2013; Revised on: 08-12-2013; Accepted on:06-01-2014

ABSTRACT

Aim: Synthesis of novel Imino-arylidene derivatives of Pyrazoline and evaluation of their *in-vitro* antimalarial activity. **Method:** It involved three steps. Initially 1-(4-aminophenyl)-3-arylprop-2-en-1-ones (**1a-1f**) were synthesized by Claisen-Schmidt condensation. Further, compounds (**1a-1f**) were refluxed with hydrazine hydrate using ethanol as solvent, to yield pyrazoline derivatives (**2a-2f**). Compounds (**2a-2f**) on refluxing with 4-methoxy benzaldeyde yield title compounds 1-(4-methoxyphenyl)-N-[4-(5-aryl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl]methanimine (**3a-3f**). The synthesized compounds were characterized by using IR, NMR and Mass spectral data. Compounds were evaluated for their *in-vitro* antimalarial activity against 3D7 *P. falciparum* using chloroquine as standard drug. **Result:** Imino-arylidene derivatives of Pyrazoline (**3a-3f**) exhibited better *in vitro* antimalarial activity against 3D7 *P. falciparum* as compared to pyrazolines (**2a-2f**). Compound **3d** was found to have IC_{50} value of 9.99µgmL^{-1}. **Conclusion:** An increase in number of methoxy group on Imino-arylidene derivatives of Pyrazoline results in an increase in *in-vitro* antimalarial activity.

Key words: Pyrazoline, Schiff base, Antimalarial

1. INTRODUCTION:

Malaria caused by unicellular protozoan parasite of *Plasmodium* species (Phylum- Apicomplexa) is a threat to public mainly in tropical and subtropical regions of the world[1]. There are four causative species, which are infectious to humans, these are: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*, of which the first one is responsible for maximum deaths[1]. Development of resistant parasites has rendered many drugs virtually useless in major regions of the world, as once resistance to a new drug emerges; it quickly spreads and usually confers cross-resistance to the entire class. Hence, it is quite essential to search new chemical entities which act on different molecular targets[2,3]. The increased incidences together with rapid emergence of multi-drug resistant strains of the parasite have made the search of novel, effective, safe and inexpensive agents quintessential for the treatment of malaria.

Pyrazolines possess an array of biological activities[4-8]. Similarly, Schiff bases also have multiple pharmacological activities[9-10]. However, there is very less literature describing the antimalarial activity of pyrazoline[11-12] and Schiff bases[13]. Considering this, we thought to synthesize pyrazolines linked with Schiff base and evaluate them for *in vitro* antimalarial activity.

The chalcones (**1a-1f**), synthesized by using Claisen-Schmidt condensation[14] were treated with hydrazine hydrate to yield amino pyrazolines (**2a-2f**). These pyrazolines on treatment with 4-methoxy benzaldehyde gave title compounds (**3a-3f**). Compounds were evaluated for their *in vitro* gametocytocidal activity against CQ-sensitive 3D7 of *P. falciparum* strain by reported method using chloroquine as standard drug [15]. *In vitro* results substantiate that dual molecules *viz.* pyrazoline-Schiff base possess better activity as compared to pyrazolines.

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2. MATERIAL AND METHODS

2.1 Experimental section

Melting points of all compounds were measured by open-end capillary method and are uncorrected. TLC was performed with silica gel 60 F_{254} (Merck) using Toulene: Ethyl Acetate: Formic Acid (5:4:1) as solvent system and the spots were located either under ultra violet light or through the exposure to iodine vapours.

The IR spectra were recorded using Bruker alpha-T spectrophotometer. ^{1}H-NMR spectra were recorded on a Bruker Avance-400MHz in DMSO-d_6 with tetramethylsilane (TMS) as internal standard. The mass spectra (MS) were recorded on Waters SYNAPT UPLC-MS/MS working on Mass Linux V4.1 software. Spectral data are consistent with assigned structures. Elemental analyses were performed on a Perkin-Elmer model 240 analyser (C, H, N) and found within the range of ±0.4% of theoretical values.

2.2 General Method

2.2.1 Synthesis of compounds 1a-1f

1-(4-Aminophenyl)-3-arylprop-2-en-1-one (**1a-1f**) were synthesized by the reported method[14].

2.2.2 Synthesis of compounds 2a-2f

Mixture of compounds (**1a-1f**) (0.01 mol) and hydrazine hydrate (0.01 mol) in absolute ethanol (25 mL) were refluxed for 36-42 hrs. After the completion of reaction, the reaction mixture was concentrated and poured into ice-cold water. Solid obtained was filtered, washed with excess of water, dried and recrystallized from ethanol (**Scheme-1**).

2.2.3 Synthesis of compounds 3a-3f

Mixture of compound (**2a-2f**) (0.01 mol) and 4-methoxy benzaldehyde (0.01 mol) was refluxed for 12-18 hrs in absolute ethanol (25 mL). On cooling, the separated solid was filtered, dried and washed with cold ethanol (**Scheme-1**).

3. SPECTRAL DISCUSSION

3.1. 4-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2a)

Yield: 64%. R_f: 0.56. IR (KBr): 3332 (NH), 3308 &3264 (NH_2), 1620 (C=N). ^{1}HNMR (DMSO-d_6): 2.96 (dd, 1H, J_{AM} = 17.6Hz and J_{AX} = 4.4Hz, H_A), 3.69 (dd, 1H, J_{MA} = 17.2Hz and J_{MX} = 11.6Hz, H_M), 5.49 (dd, 1H, J_{XM} = 11.6Hz and J_{XA} = 4.4Hz, H_A), 7.00 (d, 2H, *J*=8.4Hz, H-3,5), 7.38 (m, 3H, H-3',4',5'), 7.44 (s, 2H, D_2O exchangeable), 7.56 (m, 2H, H-2',6'), 7.84 (d, 2H, *J*=8.4Hz, H-2,6), 8.60 (bs, 1H, NH). $C_{15}H_{15}N_3$ Anal Calcd (%) C 75.92, H 6.37, N 17.71. Found (%): C 75.90, H 6.35, N 17.69.

3.2. 4-(5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2b)

Yield: 64%. Rf: 0.59. IR (KBr): 3345 (NH), 3318 & 3274 (NH_2), 1620 (C=N). ^{1}HNMR (DMSO-d_6): 2.98 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.65 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.6Hz, H_M), 3.78 (s, 3H, OCH_3), 5.46 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.8Hz, H_A), 6.95 (d, 2H, *J*=8.4Hz, H-3',5'), 7.06 (d, 2H, *J*=8.4Hz, H-3,5), 7.48 (s, 2H, D_2O exchangeable), 7.59 (d, 2H, *J*=8.4Hz, H-2',6'), 7.88 (d, 2H, *J*=8.4Hz, H-2,6), 8.48 (bs, 1H, NH). $C_{16}H_{17}N_3O$ Anal Calcd (%): C 71.89, H 6.41, N 15.72, O 5.98. Found (%): C 71.92, H 6.40, N 15.70, O 6.00

3.3. 4-(5-(3,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2c)

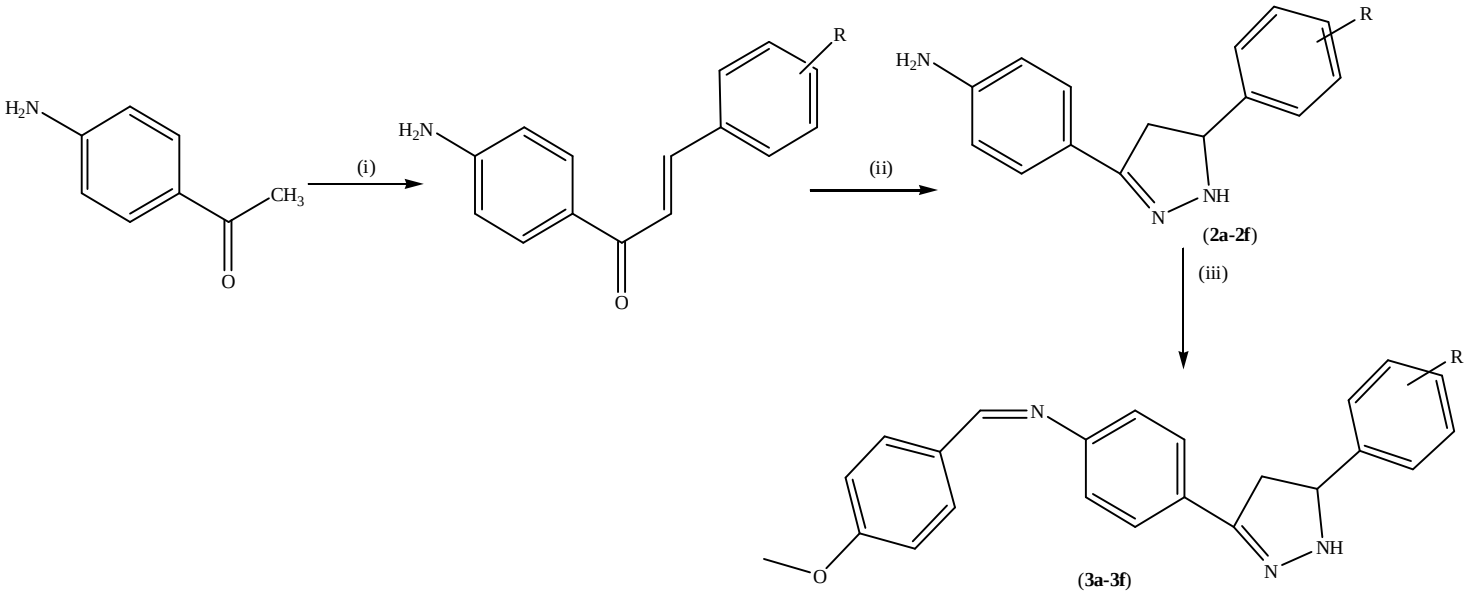
Yield: 65%. R_f: 0.61. IR (KBr): 3346 (NH), 3320 & 3276 (NH_2), 1618 (C=N). ^{1}HNMR; (DMSO-d_6): 2.94 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.62 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 3.86 (s, 6H, 2xOCH_3), 5.42 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 6.48 (s, 2H, D_2O exchangeable), 6.93 (s, 1H, H-2'), 6.97 (d, 1H, *J*=8.4Hz, H-5'), 6.98 (d, 2H, *J*=8.4Hz, H-3,5), 7.34 (d, 1H, *J*=8.4Hz, H-6'), 7.86 (d, 2H, *J*=8.4Hz, H-2,6), 8.52 (bs, 1H, NH). $C_{17}H_{19}N_3O_2$ Anal Calcd (%): C 68.67, H 6.44, N 14.13, O 10.76. Found (%): C 68.65, H 6.45, N 14.15, O 10.74.

3.4. 4-(5-(3,4,5-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2d)

Yield: 62%. R_f: 0.61. IR (KBr): 3342 (NH), 3317 & 3275 (NH_2), 1612 (C=N). ^{1}HNMR; (DMSO-d_6): 3.02 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.65 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 3.82 (s, 3H, OCH_3), 3.88 (s, 6H, 2xOCH_3), 5.54 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 6.88 (s, 2H, H-2', 6'), 6.96 (d, 2H, *J*=8.4Hz, H-3,5), 7.18 (s, 2H, D_2O exchangeable), 7.82 (d, 2H, *J*=8.4Hz, H-2,6), 8.64 (bs, 1H, NH). $C_{18}H_{21}N_3O_3$. Anal Calcd (%): C 66.04, H 6.47, N 12.84, O 14.66. Found (%): C 66.05, H 6.45, N 12.86, O 14.63.

3.5. 4-(5-(2-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2e)

Yield: 67%. R_f: 0.53. IR (KBr): 3332 (NH), 3312 & 3278 (NH_2), 1616 (C=N). ^{1}HNMR; (DMSO-d_6): 3.04 (dd, 1H, J_{AM} = 17.2Hz and J_{AX} = 4.8Hz,



Reagents and conditions: (i) Aromatic aldehydes; 5% KOH; ethanol, stirring, (ii) NH_2NH_2; absolute alcohol; reflux, (iii) Aromatic aldehyde, absolute alcohol;reflux

R= H, 4-OCH_3, 3,4-diOCH_3, 3,4,5-triOCH_3, 2-Cl, 4-NO_2

SCHEME 1

H_A), 3.68 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 5.66 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 7.04 (d, 2H, *J*=8.4Hz, H-3,5), 7.21 (s, 2H, D_2O exchangeable), 7.34-7.58 (m, 4H, H-3',4',5',6'), 7.86 (d, 2H, *J*=8.4Hz, H-2,6), 8.62 (bs, 1H, NH). $C_{15}H_{14}ClN_3$ Anal Calcd (%): C 66.30, H 5.19, Cl 13.05, N 15.46. Found (%): C 66.32 H 5.17, Cl 13.03 N 15.45.

3.6. 4-(5-(3-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzenamine (2f)

Yield: 66%. R_f: 0.55. IR (KBr): 3336 (NH), 3315 & 3272 (NH_2), 1612 (C=N). ^{1}HNMR; (DMSO-d_6): 3.12 (dd, 1H, J_{AM} = 16.8Hz and J_{AX} = 4.4Hz, H_A), 3.72 (dd, 1H, J_{MA} = 16.8Hz and J_{MX} = 10.8Hz, H_M), 5.70 (dd, 1H, J_{XM} = 10.8Hz and J_{XA} = 4.0Hz, H_A), 7.06 (d, 2H, *J*=8.0Hz, H-3,5), 7.48 (s, 2H, D_2O exchangeable), 7.82 (d, 2H, *J*=8.0Hz, H-2,6), 7.90 (dd, 1H, *J*= 8.0 & 7.6Hz, H-5'), 8.06 (d, 1H, *J*= 8.0Hz, H-6'), 8.18 (d, 1H, *J*= 7.6Hz, H-4'), 8.24 (s, 1H, H-2'), 8.56 (bs, 1H, NH). $C_{15}H_{14}N_4O_2$ Anal Calcd (%): C 63.82, H 5.00, N 19.85, O 11.34. Found (%): C 63.80, H 4.99, N 19.87, O 11.35.

3.7. 1-(4-Methoxyphenyl)-N-[4-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl]methanimine (3a)

Yield: 68% MP: 210-12°C. R_f: 0.50. IR (KBr): 3346 (NH), 1620 (C=N). ^{1}HNMR; (DMSO-d_6): 3.02 (dd, 1H, J_{AM} = 17.6Hz and J_{AX} = 4.4Hz, H_A), 3.72 (dd, 1H, J_{MA} = 17.2Hz and J_{MX} = 11.6Hz, H_M), 3.88 (s, 3H, OCH_3), 5.62 (dd, 1H, J_{XM} = 11.6Hz and J_{XA} = 4.4Hz, H_A), 6.90 (d, 2H, J=8.8Hz, H-3",5"), 6.96 (d, 2H, *J*=8.4Hz, H-3,5), 7.42-7.54 (m, 5H, H-2',3',4',5',6'), 7.76 (d, 2H, *J*=8.4Hz, H-2,6), 7.82 (d, 2H, J=8.8Hz, H-2",6"), 8.02 (s, 1H, CH=N), 8.52 (bs, 1H, NH). Mass: m/z; (M^++1) 356. $C_{23}H_{21}N_3O$ Anal Calcd (%): C 77.72, H 5.96, N 11.82, O 4.50. Found (%): C 77.75, H 5.94 N 11.80, O 4.48.

3.8. N-{4-[5-(4-Methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (3b)

Yield: 72%. MP: 228-230. R_f: 0.55. IR (KBr): 3356 (NH), 1624 (C=N). ^{1}HNMR; (DMSO-d_6): 3.04 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.68 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.6Hz, H_M), 3.84 (s, 6H, 2xOCH_3), 5.62 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.8Hz, H_A), 6.94 (d, 2H, J=8.8Hz, H-3",5"), 7.01 (d, 2H, *J*=8.4Hz, H-3',5'), 7.26 (d, 2H, *J*=8.4Hz, H-3,5), 7.52 (d, 2H, *J*=8.4Hz, H-2',6'), 7.78 (d, 2H, *J*=8.4Hz, H-2,6), 7.86 (d, 2H, J=8.8Hz, H-2",6"), 8.08 (s, 1H, CH=N), 8.94 (bs, 1H, NH). Mass: m/z; (M^++1) 386. $C_{24}H_{23}N_3O_2$ Anal Calcd (%): C 74.78, H 6.01, N 10.90, O 8.30. Found (%): C 74.80, H 6.02, N 10.92, O 8.28.

3.9. N-{4-[5-(3,4-Dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (3c)

Yield: 66%. MP: 220-22°C. R_f: 0.58. IR (KBr): 3348 (NH), 1612 (C=N). ^{1}HNMR; (DMSO-d_6): 3.05 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.64 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 3.86 (s, 6H, 2xOCH_3), 3.92 (s, 3H, OCH_3), 5.66 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 6.90 (d, 2H, *J*=8.4Hz, H-3,5), 6.94 (s, 1H, H-2'), 6.99 (d, 1H, *J*=8.4Hz, H-5'), 7.02 (d, 2H, J=8.8Hz, H-3",5"), 7.26 (d, 1H, *J*=8.4Hz, H-6'), 7.80 (d, 2H, *J*=8.4Hz, H-2,6), 7.90 (d, 2H, J=8.8Hz, H-2",6"), 7.98 (s, 1H, CH=N), 8.58 (bs, 1H, NH). Mass: m/z; (M^++1) 416. $C_{25}H_{25}N_3O_3$ Anal Calcd (%): C 72.27, H 6.06, N 10.11, O 11.55. Found (%): C 72.25, H 6.05, N 10.11, O 11.57.

3.10. N-{4-[5-(3,4,5-Trimethoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (3d)

Yield: 64%. MP: 201-02°C. R_f:).57. IR (KBr): 3352 (NH), 1620 (C=N). ^{1}HNMR; (DMSO-d_6): 3.10 (dd, 1H, J_{AM} = 18.0Hz and J_{AX} = 4.4Hz, H_A), 3.68 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 3.80 (s, 3H, OCH_3), 3.84 (s, 6H, 2xOCH_3), 3.87 (s, 3H, OCH_3), 5.58 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 6.92 (s, 2H, H-2', 6'), 6.90 (d, 2H, *J*=8.4Hz, H-3,5), 7.04 (d, 2H, J=8.8Hz, H-3",5"), 7.78 (d, 2H, *J*=8.4Hz, H-2,6), 7.84 (d, 2H, J=8.8Hz, H-2",6"), 8.01 (s, 1H, CH=N), 8.56 (bs, 1H, NH). Mass: m/z; (M^++1) 446. $C_{26}H_{27}N_3O_4$ Anal Calcd (%): C 70.09, H 6.11, N 9.43, O 14.37. Found (%): C 70.10, H 6.10, N 9.45, O 14.35.

3.11. N-{4-[5-(2-Chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (3e)

Yield: 70%. MP: 211-12°C. R_f: 0.50. IR (KBr): 3342 (NH), 1626 (C=N). ^{1}HNMR; (DMSO-d_6): 3.08 (dd, 1H, J_{AM} = 17.2Hz and J_{AX} = 4.8Hz, H_A), 3.69 (dd, 1H, J_{MA} = 17.6Hz and J_{MX} = 11.2Hz, H_M), 3.84 (s, 3H, OCH_3), 5.68 (dd, 1H, J_{XM} = 11.2Hz and J_{XA} = 4.4Hz, H_A), 7.08 (d, 2H, *J*=8.4Hz, H-3,5), 7.14 (d, 2H, J=8.8Hz, H-3",5"), 7.42-7.56 (m, 4H, H-3',4',5',6'), 7.78 (d, 2H, *J*=8.4Hz, H-2,6), 7.82 (d, 2H, J=8.8Hz, H-2",6"), 7.98 (s, 1H, CH=N), 8.55 (bs, 1H, NH). Mass: m/z; (M^++1) 390. $C_{23}H_{20}ClN_3O$ Anal Calcd (%): C 70.85, H 5.17, Cl 9.09, N 10.78, O 4.10. Found (%): C 70.83, H 5.15, Cl 9.10, N 10.80, O 4.08.

3.12. N-{4-[5-(3-Nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (3f)

Yield: 62%. MP: 231-32°C. R_f: 0.49. IR (KBr): 3338 (NH), 1622 (C=N). ^{1}HNMR; (DMSO-d_6): 3.10 (dd, 1H, J_{AM} = 16.8Hz and J_{AX} = 4.4Hz, H_A), 3.68 (dd, 1H, J_{MA} = 16.8Hz and J_{MX} = 10.8Hz, H_M), 3.82 (s, 3H, OCH_3), 5.72 (dd, 1H, J_{XM} = 10.8Hz and J_{XA} = 4.0Hz, H_A), 7.04 (d, 2H, *J*=8.0Hz, H-3,5), 7.12 (d, 2H, J=8.8Hz, H-3",5"), 7.80 (d, 2H, *J*=8.0Hz, H-2,6), 7.84 (d, 2H, J=8.8Hz, H-2",6"), 7.92 (dd, 1H, *J*= 8.0 & 7.6Hz, H-5'), 8.02 (s, 1H, CH=N), 8.10 (d, 1H, *J*= 8.0Hz, H-6'), 8.22 (d, 1H, *J*= 7.6Hz, H-4'), 8.26 (s, 1H, H-2'), 8.48 (bs, 1H, NH). Mass: m/z; (M^++1) 401. $C_{23}H_{20}N_4O_3$ Anal Calcd (%): C 68.99, H 5.03, N 13.99 O 11.99. Found (%): C 69.00, H 5.05, N 13.97, O 12.01.

4. PHARMACOLOGY

The compounds (**2a-2f** and **3a-3f**) were evaluated for their antimalarial activity by Dua *et al* method[15]. The activity was checked in gametocyte producing *P. falciparum* culture lines (FDL-HD). Culture was maintained in *in-vitro* O+ve RBC at 10% haematocrit in AB+ve serum in RPMI 1640 medium supplemented with d-glucose and l-glutamine. The culture was treated with selected concentrations of different compounds. This was allowed to grow at 37°C in carbon dioxide incubator for 72h. After incubation, blood smears were prepared and stained with Giemsa stain. Percentage inhibition for gametocytes and asexual stages was calculated by comparing growth in control sets. Chloroquine was used as a standard reference. The inhibitory concentration values which kills 50% of the parasites (IC_{50}) was considered for anti-plasmodial activity.

5. RESULT

In the present study we report the synthesis of pyrazoline- Schiff

bases hybrids. These compounds were evaluated for their *in vitro* antimalarial potential (**Table-1**). Studies suggest that Imino-arylidene derivatives of Pyrazoline (**3a-3f**) exhibited better *in vitro* antimalarial activity against 3D7 *P. falciparum* as compared to pyrazolines (**2a-2f**). Compound **3d** was found to have IC_{50} value of 9.99µgmL^{-1}.

Table 1. *In vitro* antimalarial activity of compounds 2a-2f and 3a-3f

Sr. No.	Compound	IC_{50} (µgmL^{-1})
1	2a	18.48
2	2b	16.09
3	2c	14.36
4	2d	12.89
5	2e	27.90
6	2f	32.45
7	3a	15.57
8	3b	13.25
9	3c	11.01
10	3d	9.99
11	3e	24.02
12	3f	29.90

6. DISCUSSION

The synthesized compounds were evaluated on the basis of spectral data i.e. IR, NMR and Mass. C=N stretching vibration at 1612-1603cm^{-1} in IR spectra is suggestive of the formation of pyrazolines due to ring closure. In ^{1}H-NMR spectra, the three protons H_A, H_M and H_X of pyrazoline ring appeared as doublets of doublets.

The imine-arylidne linkage of compounds **3a-f** formation is confirmed by IR and NMR spectral data. In IR spectral data disappearance of NH_2 peak indicates the formation of Schiff's base. Similarly, In ^{1}H NMR, presence of a singlet around δ 8.05 indicates the formation of benzylidene i.e. Schiff's base. The structure of the compounds was further supported by mass spectral data.

The synthesized compounds were evaluated for *in vitro* antimalarial activity. Hybrid molecules showed better inhibitory profiles compared to pyrazolines. Results also indicate that compounds having hydrophobic substitution exhibit better inhibitory profiles, as suggested by compounds **3d** and **2d**.

7. CONCLUSION

To sum up, *N*-{4-[5-(3,4,5-Trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl}-1-(4-methoxyphenyl)methanimine (**3d**) was found to have good *in vitro* antimalarial activity. An increase in number of methoxy group on Imino-arylidene derivatives of Pyrazoline results in an increase in *in-vitro* antimalarial activity. Further studies to acquire more information about the quantitative structure–activity relationship (QSAR) are in progress in our laboratory.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

ACKNOWLEDGEMENT

Authors wish to acknowledge the financial support provided by CSIR, New Delhi; Jamia Hamdard, for providing research laboratory and instrumentation facility (NMR, Mass and IR) at the institute; National Institute of Malaria Research, New Delhi for carrying out *in vitro* antimalarial activity.

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Source of support: Nil, Conflict of interest: None Declared