IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
February 2017 Vol.:8, Issue:3

Synthesis, Characterisation and Antimalarial Activity of Some New 3-Benzyl-2-Thioxothiazolidin-4-One Derivatives

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Mehul Zaveri* **and Neha Kawathekar**

Department of Pharmacy, Shri G.S institute of Technology and Science, 23- Park Road, Indore (MP) India - 452003

Submission: 7 February 2017
Accepted: 12 February 2017
Published: 25 February 2017

Keywords: 3-benzyl-2-thioxothiazolidin-4-one,Antimalarial activity

ABSTRACT

In present investigation, a series of new 3-benzyl-2-thioxothiazolidin-4-one **(F_1-F_{11})** derivatives, have been synthesized using conventional and microwave-assisted technique. All the synthesized compounds were characterized by IR, ^{1}HNMR and Mass spectroscopy, further, these compounds were evaluated for *in-vitro* antimalarial activity by microdilution technique against resistance strains of *Plasmodium falciparum*. The result of antimalarial activity revealed that out of entire compounds, six compounds (**F_1**, **F_7**, **F_8**, **F_9**, **F_{10}**, & **F_{11}**) exhibited the IC_{50} values ranging from 0.8–1.2µg/ml, four compounds (**F_2**, **F_3**, **F_5** and **F_6**) displayed antimalarial activity IC_{50} values in the range of 0.7-0.8µg/ml, and one compound (**F_4**) showed most significant result with maximum IC_{50} value of 0.7µg/ml, thus it could be identified as structural lead for further development of new antimalarial agents.

1. INTRODUCTION

Malaria is one of the world's most common and severe tropical diseases. It is caused by a protozoan belonging to the genus *Plasmodium* and transmitted by the anopheles mosquito. The problem of widespread malaria continues unabated worldwide, as the disease is present in over 104 countries. World Health Organization (WHO) estimates half of the world's population is at risk of malaria. Globally, 300–500 million episodes of malarial illnesses occur each year, resulting in over one million deaths from this devastating disease (1, 2). Even with decades of research and the victorious progress of combination therapy, malaria remains one of the most serious health problems worldwide, especially in developing countries where it has huge economic and social costs. (3, 4) The distribution of drug-resistant parasite and resistant malaria infections was reported across the globe. South America and the African subcontinent were the most deadly endemic areas with resistance reported to more than just chloroquine (CQ) (Figure a), sulphadoxine-pyrimethamine combinations and Mefloquine (Figure b). (5, 6) The development of drug resistance has become a major health concern and has stimulated the search for alternative antimalarial agents. In this perspective rhodanine nucleus offers an alternative due to presence of wide spectrum of activities such as antibacterial (7), anti-inflammatory (5), antiviral (8, 9), antidiabetic (10), anticancer (11), tyrosinase inhibitors (5) and antimalarial (12) are frequently associated with low toxicity and they can be considered as a privileged scaffold and an ideal framework for the design of compounds that can interact with different targets as their inherent affinity for several biological targets (5). A series of new 3-benzyl-2-thioxothiazolidin-4-one have been synthesized and evaluated for their *in-vitro* antimalarial activities against resistant strain of *Plasmodium falciparum*.

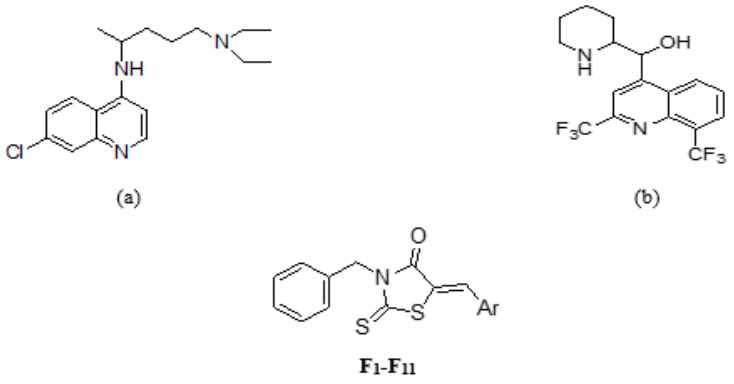


Fig.1 (a) Chloroquine, (b) Mefloquine and (F_1-F_{11}) 3-benzyl-2 thioxothiazolidin-4-one derivatives

Here in synthesis, characterization and antimalarial activity of eleven new 3-benzyl-2-thioxothiazolidin-4-one derivatives **(F_1 to F_{11})** are reported.

2. MATERIALS AND METHODS

Melting points were determined by open capillary method and are uncorrected. The progress of the reactions was monitored by thin layer chromatography (TLC) with ethyl acetate: hexane (1:1 v/v) as eluent. TLC was carried out on precoated plates (silica gel 60, F254) and visualized with UV light. Column chromatography was performed on silica gel (100-200). Anton Paar, Monowave 300, Microwave synthesis reactor was used for microwave-assisted synthesis. Infrared spectra were determined as KBr pellets on a Shimadzu IR affinity-1 model 1400 spectrophotometer and are expressed in cm^{-1}. ^1H NMR spectra were recorded on a Bruker's Avance-III FT NMR spectrometers using $CDCl_3$ as solvent; chemical shifts are expressed in δ (ppm). HRMS spectral data were obtained with a Bruker micro, TOF QII high-resolution mass spectrometer and both the above analysis were performed at Indian Institute of Science Education and Research Technology (IISER, Bhopal); IR analyses were performed in Shri Govindram Seksaria Institute of Technology and Science (S.G.S.I.T.S., Indore M. P).

2.1 *Synthesis*

General procedure for Synthesis of 3-benzyl-2-thioxothiazolidin-4-one intermediate (I_1)

An equimolar amount of carbon disulfide was added dropwise to an ice-cold solution of benzylamine (1) and triethylamine in ethyl acetate over 30 min (Scheme 1). After stirring overnight, a yellow dithiocarbamate was isolated by filtration and reacted with an equimolar amount of aqueous bromoacetic acid solution ($NaHCO_3$, pH 8-9). After 2 hours, the solution was acidified (HCl), refluxed and the resultant precipitate was crystallized from ethanol to yield 3-benzyl-2-thioxothiazolidin-4-one (I_1).

General procedure for synthesis of F_1-F_{11}

A mixture of 2-thiaoxo-4-thiazolidinone intermediate **I_1** (0.2 mmol), substituted aromatic/ heteroaromatic aldehydes (0.2 mmol), and three drops of piperidine in absolute ethanol (5 ml) were thoroughly mixed in a glass vial (G10/G30). The reaction mixture was then heated with microwave irradiation at 100^0C for 25 min (table 2). After cooling, the solid mass was placed in 50ml of cold ethanol and crushed ice. The slurry was filtered to give solid mass and dried under vacuum to give corresponding $S_4I_1F_1$-F_6 and $S4I_1F_9$-F_{13} derivatives.

Table 1: Structure, Molecular formula, Molecular weight, % Yield, Melting point and antimalarial activity (IC_{50} µg/ml) of F_1- F_{11} derivatives

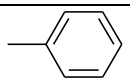
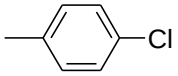
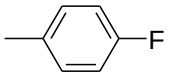
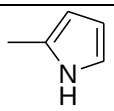
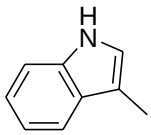
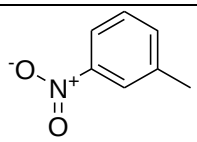
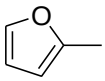
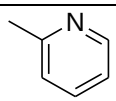
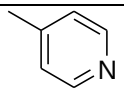
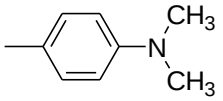
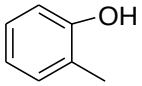
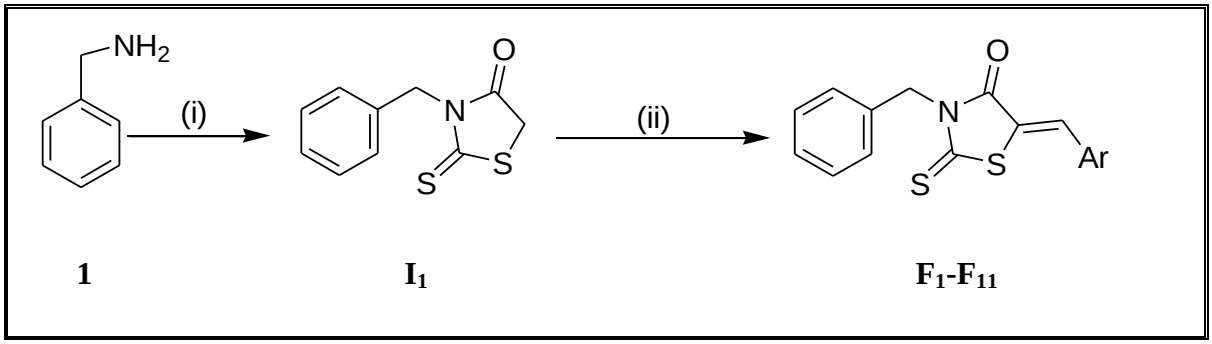
S. No	Comp. Code	substituents Ar	Molecular Formula	Molecular Weight	% yield	Melting Point ^0C	IC_{50} µg/ml
1.	**F_1**		$C_{17}H_{13}NOS_2$	311.42	76	170-172	1.15
2.	**F_2**		$C_{17}H_{12}ClNOS_2$	345.87	85	160-162	0.78
3.	**F_3**		$C_{17}H_{12}FNOS_2$	329.41	82	140-142	0.76
4.	**F_4**		$C_{15}H_{12}N_2OS_2$	300.4	79	218-220	0.70
5.	**F_5**		$C_{19}H_{14}N_2OS_2$	350.46	78	260-262	0.75
6.	**F_6**		$C_{17}H_{12}N_2O_3S_2$	356.42	84	188-190	0.76
7.	**F_7**		$C_{15}H_{11}NOS_3$	317.45	78	166-168	0.90
8.	**F_8**		$C_{16}H_{12}N_2OS_2$	312.41	85	182-184	1.20
9.	**F_9**		$C_{16}H_{12}N_2OS_2$	312.41	84	150-152	0.92
10.	**F_{10}**		$C_{19}H_{18}N_2OS_2$	354.49	85	184-186	0.85
11.	**F_{11}**		$C_{18}H_{13}NO_2S_2$	339.43	77	196-198	0.94
12.	**CQ**	-	-	-	-	-	0.020
13.	**Quinine**	-	-	-	-	-	0.268

Table 2: Experiment Setting and Method for Microwave synthesis reactor

Step	Program	Temperature	Time	Cooling	Stirrer Speed
		°C	mm: ss		Rpm
1.	Heat as fast as possible	100	-	Off	600
2.	Hold	-	25:00	Off	600
3.	Cool down	55	0	On	600



1 **I_1** **F_1-F_{11}**

Scheme No. 1: Reagents and Conditions (i) (a) CS_2, TEA, EtOAc, rt, 12 h; (b) $BrCH_2COOH$, $NaHCO_3$, rt, 2h ; (c) HCl, reflux, 2 h; (ii) Piperidine, ethanol, MW,100^o C, 25 Min.

2-thiaoxo-4-thiazolidinone intermediate (I_1)

Orange crystal; IR (KBr) cm^{-1}; 2969.54 (C-H, stretch, aromatic), 1737.94 (C=O), 1602.91 (C=S), 1496.83 (C=C, aromatic), 846.79 (C-H, bend, aromatic); ^{1}H NMR ($CDCl_3$): 7.40 (d, 2H, N-benzyl), 7.27 (t, 3H, N-benzyl), 5.16 (s, 2H, CH_2), 3.93 (s, 2H, CH_2).

(Z)-3-benzyl-5-benzylidene-2-thioxothiazolidin-4-one (F_1)

Orange crystal; IR (KBr) cm^{-1}; 3033.19 (=C-H, stretch), 2984.97 (C-H, stretch, aromatic), 1710.93 (C=O), 1605.81 (C=S), 1583.63 (C=C, aromatic), 818.82 (C-H, bend, aromatic); ^{1}H NMR ($CDCl_3$): 7.72 (s, 1H, =CH), 7.46–7.47 (m, 5H, phenyl), 7.30 (t, 3H, N-benzyl), 7.24 (d, 2H, N-benzyl), 5.31 (s, 2H, CH_2); HRMS (ESI$^+$) (m/z): [M+1], 312.1.

(Z)-5-(4-chlorobenzylidene)-3-benzyl-2-thioxothiazolidin-4-one (F_2)

Orange crystal; IR (KBr) cm^{-1}; 3032.23 (=C-H, stretch), 2984.97 (C-H, stretch, aromatic), 1710.93 (C=O), 1605.81 (C=S), 1583.63 (C=C, aromatic), 818.82 (C-H, bend, aromatic), 753.23 (C-Cl); ^{1}H NMR ($CDCl_3$): 7.65 (s, 1H, =CH), 7.45 (d, 2H, Chloro phenyl), 7.43 (d,

2H, Chloro phenyl), 7.38 (d, 1H, N-benzyl), 7.30 (d, 1H, N-benzyl), 7.26 (t, 3H, N-Benzyl), 5.30 (s, 2H, CH_2); HRMS (ESI^+) (m/z): [M+1], 346.87

(Z)-5-(4-bromobenzylidene)-3-benzyl-2-thioxothiazolidin-4-one (F_3)

Orange crystal; IR (KBr) cm^{-1}; 3063.09 (=C-H, stretch), 2946.39 (C-H, stretch, aromatic), 1702.25 (C=O), 1595.20 (C=S), 1507.43 (C=C, aromatic), 828.46 (C-H, bend, aromatic), 757.09 (C-Br); ^1H NMR ($CDCl_3$): 7.68 (s, 1H, =CH), 7.47 (d, 2H, bromo phenyl), 7.43 (d, 2H, bromo phenyl), 7.30 (d, 1H, N-benzyl), 7.26 (d, 1H, N-benzyl), 7.13 (t, 3H, N-Benzyl), 5.30 (s, 2H, CH_2); HRMS (ESI^+) (m/z): [M+1], 330.41

(E)-5-((1H-pyrrol-2-yl) methylene)-3-benzyl-2-thioxothiazolidin-4-one (F_4)

Orange crystal; IR (KBr) cm^{-1}; 3028.37 (=C-H, stretch), 2994.62 (C-H, stretch, aromatic), 1684.89 (C=O), 1598.13 (C=S), 1551.8 (C=C, aromatic), 822.68 (C-H, bend, aromatic), 3326.39 (N-H); ^1H NMR ($CDCl_3$): 7.58 (s, 1H, =CH), 7.42 (d, 2H, N-benzyl), 7.27 (t, 3H, N-benzyl), 7.24 (d, 2H, pyrrole), 6.43 (t, 1H, pyrrole); 8.66 (s, 1H, NH-pyrrole), 5.30 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1]: 301.1.

(E)-5-((1H-indol-2-yl) methylene)-3-benzyl-2-thioxothiazolidin-4-one (F_5)

Orange crystal; IR (KBr) cm^{-1}; 3058.27 (=C-H, stretch), 2931.93 (C-H, stretch, aromatic), 1681.04 (C=O), 1599.06 (C=S), 1574.95 (C=C, aromatic), 814.00 (C-H, bend, aromatic), 1228.71 (C-N);^1H NMR ($CDCl_3$): 8.78 (s, 1H, NH-Indole), 7.83 (d, 2H, N-phenyl), 8.10 (s, 1H, =CH), 7.48 (t, 3H, N-phenyl), 7.42 (d, 2H, Indole), 7.30 (t, 2H, Indole), 5.32 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1], 352.46

(Z)-5-(3-nitrobenzylidene)-3-benzyl-2-thioxothiazolidin-4-one (F_6)

Yellow crystal; IR (KBr) cm^{-1}; 3063.09 (=C-H, stretch), 2977.26 (C-H, stretch, aromatic), 1715.76 (C=O), 1602.91 (C=S), 1534.44(C=C, aromatic), 826.53 (C-H, bend, aromatic), 1379.16 (-NO2); ^1H NMR ($CDCl_3$): 8.32 (s, 1H, NO_2-phenyl),, 8.25 (d, 1H, NO_2-phenyl), 7.72-7.77 (t, 2H, NO_2-phenyl), 7.441 (d, 2H, N-benzyl), 7.28-7.33 (t, 3H, N-benzyl), 7.24 (s, 1H, =CH), 5.31 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1], 357.42

(E)-3-benzyl-5-(thiophen-2-ylmethylene)-2-thioxothiazolidin-4-one (F_7)

Yellow crystal; IR (KBr) cm^{-1}; 3081.42 (=C-H, stretch), 2941.57 (C-H, stretch, aromatic), 1707.08 (C=O), 1593.27 (C=S), 1495.86 (C=C, aromatic), 848.72 (C-H, bend, aromatic); ^1H

NMR ($CDCl_3$): 7.89 (s, 1H CH), 7.67 (d, 2H, N-benzyl), 7..38 (d, 2H, Thiophen), 7.28 (t, 3H, N-benzyl), 7.16 (t, 1H, Thiophen), 5.29 (s, 2H, CH_2); HRMS (ESI^+) (m/z): [M+1], 318.45

(Z)-3-benzyl-5-(pyridin-2-ylmethylene)-2-thioxothiazolidin-4-one (F_8)

Orange crystal; IR (KBr) cm^{-1}; 3033.19 (=C-H, stretch), 2942.53 (C-H, stretch, aromatic), 1703.22 (C=O), 1609.67 (C=S), 1582.66 (C=C, aromatic), 816.89 (C-H, bend, aromatic), 1679.11 (C=N) ; ^1H NMR ($CDCl_3$): 8.74 (s, 1H, =CH), 7.71-7.76 (d, 2H, Pyridine), 7.43 (d, 2H, N-benzyl), 7.26 (t, 3H, N-benzyl), 7.23 (t, 2H, Pyridine), 5.31 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1], 313.41

(Z)-3-benzyl-5-(pyridin-4-ylmethylene)-2-thioxothiazolidin-4-one (F_9)

Red crystal; IR (KBr) cm^{-1}; 3024.51 (=C-H, stretch), 2900.1(C-H, stretch, aromatic), 1707.08 (C=O), 1592.31(C=S), 1546.01 (C=C, aromatic), 806.28 (C-H, bend, aromatic), 1667.53 (C=N) ; ^1H NMR ($CDCl_3$): 8.71 (d, 2H, Pyridine), 7.59 (s, 1H, =CH), 7.43 (d, 2H, Pyridine), 7.29 (m, 5H, N-benzyl), 5.30 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1], 313.41

(Z)-5-(4-(dimethylamino)benzylidene)-3-benzyl-2-thioxothiazolidin-4-one (F_{10})

Red crystal; IR (KBr) cm^{-1}; 3083.34 (=C-H, stretch), 3002.33 (C-H, stretch, aromatic), 1696.47 (C=O), 1609.67 (C=S), 1584.59 (C=C, aromatic), 841.96 (C-H, bend, aromatic), ; ^1H NMR ($CDCl_3$): 7.65 (s, 1H, =CH), 7.45 (d, 2H, N-benzyl), 7.36 (d, 2H, N-benzyl), 7.26 (t, 3H, N-benzyl), 6.69 (d, 2H, N-benzyl), 5.30 (s, 2H, CH_2), 3.05 (s, 6H CH_3),; HRMS (ESI^+) (m/z) : [M+1] 355.1

(Z)-5-(2-hydroxybenzylidene)-3-benzyl-2-thioxothiazolidin-4-one (F_{11})

Red crystal; IR (KBr) cm^{-1}3245.37 (OH), 3031.26 (=C-H), 1679.11 (C=O), 1588.45 (C=S), 1493.93 (C=C, aromatic), 807.24 (C-H, bend, aromatic); ^1H NMR ($CDCl_3$): 8.13 (s, 1H, OH), 7.90 (s, 1H, =CH), 7.46-7.52 (t, 3H, N-benzyl), 7.34 (t, 2H, OH-Phenyl), 7.27 (d, 2H, N-benzyl), 7.25 (d, 1H, OH-Phenyl), 6.81 (s, 1H, OH-Phenyl), 5.31 (s, 2H, CH_2); HRMS (ESI^+) (m/z) : [M+1], 340.43.

Antimalarial evaluation

All the synthesized compounds were screened for *in vitro* antimalarial activity at Microcare laboratory & TRC, Surat, Gujarat. The *in-vitro* antimalarial assay was carried out in 96 well microtiter plates according to the microassay protocol of Rieckmann and co-workers with

minor modifications [ ]. All the cultures of *P. falciparum* strains were maintained in medium RPMI1640 supplemented with 25m MHEPES, 1% D-glucose, 0.23% sodium bicarbonate and 10% heat-inactivated human serum. The asynchronous parasites of *P. falciparum* were synchronized after 5% D-sorbitol treatment to obtain only the ring stage parasitized cells. For carrying out the assay, an initial ring stage parasitaemia of 0.8 to 1.5% at 3% haematocrit in a total volume of 200µl of medium RPMI-1640 was determined by samples, prepared in DMSO and their subsequent dilutions were prepared with culture Jaswant Singh Bhattacharya (JSB) staining to assess the percent parasitaemia (rings) and maintained with 50 % RBCs (O+). A stock solution of 5 mg/ml of each of the test samples was prepared in DMSO and subsequent dilutions were prepared with culture medium, then diluted samples were added to the test wells so as to obtain final concentrations ranging between 0.4µg/ml-100µg/ml in duplicate well-containing parasite cell preparation. The culture plates were incubated at 37^0C in a candle jar, after 36-40 hours of incubation; thin blood smear slides were prepared from each well and stained with JSB stain. The slides were observed under microscope to record maturation of ring stage parasites into trophozoites and schizonts in presence of different concentrations of the test agents. The test concentration which inhibited the complete maturation into schizonts was recorded as the IC_{50} value of test compounds.

4. RESULTS AND DISCUSSION

4.1 *Chemistry*

Commercially available benzylamine (1) was reacted with carbon disulfide, followed by reaction with bromoacetate and acidic cyclization to give 3-benzyl-2-thioxothiazolidin-4-one intermediate (I_1) (Scheme 1). These intermediates upon Knoevenagel condensation with suitably substituted aromatic/heteroaromatic aldehydes in ethanol under microwave heating condition in presence of piperidine produced analogs F_1-F_{11} (table 1). This reaction generated a double bond that produced E and Z isomers. Similar analogs are reported to exist predominantly as Z-isomers. (5, 6) it is presumed that the analogs synthesized here are mainly Z-isomers.

4.2 Antimalarial activity

All the compounds were screened for intraerythrocytic *in vitro* antimalarial activity against resistance strains of *Plasmodium falciparum* by using chloroquine and quinine as reference drugs. The results of antimalarial activity are summarized in table 1. Among the eleven

evaluated compounds, four compounds (**F_2, F_3, F_5** and **F_6)** displayed antimalarial activity (IC_{50} values) in the range of 0.7-0.8µg/ml, six compounds (**F_1**, **F_7**, **F_8**, **F_9**, **F_{10}**, & **F_{11}**) exhibited the IC_{50} values ranging from 0.8–1.2µg/ml and one compound (**F_4)** showed most significant result with maximum IC_{50} value of 0.7µg/ml. Variations of different substituent on the aromatic ring and replacement of aromatic ring with heterocyclic ring have been explored to ascertain the structure-activity relationship among the synthesized compounds. Compounds with 3-nitro (compound **F_6**, IC_{50}: 0.76µg/ml) and 2-hydroxyl (compound **F_{11}**, IC_{50}: 0.94µg/ml) substitutions on phenyl ring leads to marginal increase in potency compared to an unsubstituted compound **F_1**. Replacement by 4-pyridine appeared to potentiate antimalarial activity and by 2-pyridine leads to reduction in potency. With reference to the compound **F_1** (IC_{50}: 1.15µg/ml) substitution with chloro (compound **F_2**, IC_{50}: 0.78µg/ml) or fluoro (compound **F_3**, IC_{50}: 0.76µg/ml) or *N*, *N*, dimethyl (compound **F_{10}**, IC_{50}: 0.85µg/ml) at para position of phenyl ring appeared to potentiate antimalarial activity. Replacement of phenyl ring with heterocyclic ring like Pyrrole (compound **F_4**, IC_{50}: 0.70µg/ml), Indole (compound **F_5**, IC_{50}: 0.75 µg/ml), Furan (compound **F_7**, IC_{50}: 0.90µg/ml) leads to significant increase in antimalarial activity.

5. CONCLUSION

There is a dire need for development of effective and highly potent antimalarial agents after widespread development of resistance to currently available antimalarial drugs. As part of our research, we have synthesized a series of eleven new 3-benzyl-2-thioxothiazolidin-4-one (F_1-F_{11}) derivatives, using conventional and microwave-assisted technique. All the compounds were confirmed by IR, ^{1}HNMR and mass spectral data and screened for antimalarial activity. One compound **(F_4)** showed most significant result with maximum IC_{50} value of 0.7µg/ml against resistant strain of *plasmodium falciparum*. Further exploration and optimization of 3-benzyl-2-thioxothiazolidin-4-one derivatives could be useful for future development of novel antimalarial molecules.

ACKNOWLEDGMENTS

The authors are grateful to Director, S. G. S. I. T. S., Indore for providing facilities for successful completion of above work.

REFERENCES

1. Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW. The global distribution and population at risk of malaria: past, present, and future. Lancet Infect Dis. 2004;4(6):327-36.
2. Lou J, Lucas R, Grau GE. Pathogenesis of cerebral malaria: recent experimental data and possible applications for humans. Clin Microbiol Rev. 2001;14(4):810-20.
3. Liehl P, Mota MM. Innate recognition of malarial parasites by mammalian hosts. International journal for parasitology. 2012;42(6):557-66.
4. Sibley CH, Price RN. Monitoring antimalarial drug resistance: Applying lessons learned from the past in a fast-moving present. International journal for parasitology Drugs and drug resistance. 2012;2:126-33.
5. Cutshall NS, O'Day C, Prezhdo M. Rhodanine derivatives as inhibitors of JSP-1. Bioorganic & Medicinal Chemistry Letters. 2005;15(14):3374-9.
6. Sing WT, Lee CL, Yeo SL, Lim SP, Sim MM. Arylalkylidene rhodanine with bulky and hydrophobic functional group as selective HCV NS3 protease inhibitor. Bioorganic & Medicinal Chemistry Letters. 2001;11(2):91-4.
7. AbdelKhalek A, Ashby CR, Jr., Patel BA, Talele TT, Seleem MN. In Vitro Antibacterial Activity of Rhodanine Derivatives against Pathogenic Clinical Isolates. PloS one. 2016;11(10):e0164227.
8. Kamila S, Ankati H, Biehl ER. An efficient microwave assisted synthesis of novel class of Rhodanine derivatives as potential HIV-1 and JSP-1 inhibitors. Tetrahedron letters. 2011;52(34):4375-7.
9. Ramkumar K, Yarovenko VN, Nikitina AS, Zavarzin IV, Krayushkin MM, Kovalenko LV, et al. Design, synthesis and structure-activity studies of rhodanine derivatives as HIV-1 integrase inhibitors. Molecules. 2010;15(6):3958-92.
10. Murugan R, Anbazhagan S, Lingeshwaran, Sriman Narayanan S. Synthesis and in vivo antidiabetic activity of novel dispiropyrrolidines through [3+2] cycloaddition reactions with thiazolidinedione and rhodanine derivatives. Eur J Med Chem. 2009;44(8):3272-9.
11. Azizmohammadi M, Khoobi M, Ramazani A, Emami S, Zarrin A, Firuzi O, et al. 2H-chromene derivatives bearing thiazolidine-2,4-dione, rhodanine or hydantoin moieties as potential anticancer agents. Eur J Med Chem. 2013;59:15-22.
12. Kumar G, Parasuraman P, Sharma SK, Banerjee T, Karmodiya K, Surolia N, et al. Discovery of a rhodanine class of compounds as inhibitors of Plasmodium falciparum enoyl-acyl carrier protein reductase. Journal of Medicinal Chemistry. 2007;50(11):2665-75.