# Synthesis, Characterization and Anti-Malarial activity of [3-(5-methylfuran-2-carbonyl)-1-phenyl-4,5-dihydro-1*h*-pyrazol-5-yl](substituted-phenyl)methanone

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**Abstract**

Malaria is a growing infectious disease burden due to the increasing emergence of resistant strains of Plasmodium falciparum. Because of the limited therapeutic efficacy of available antimalarial drugs, the development of potent antimalarial drug agents is therefore an urgent requirement to fight against resistant malaria. The objective of this work was to develop novel Pyrazolines based antimalarial agents that would be active for malaria. Some pyrazoline derivatives were synthesized for the evaluation of their potential as possible antimalarial agents, particularly against resistant malaria. The antimalarial activity of synthesized compounds was evaluated in vitro against blood stage parasites of P. falciparum. Results reveal the in vitro antimalarial activity of synthesized 7[5-(2-chlorobenzoyl)-1-phenyl-4,5-dihydro-1H pyrazol-3-yl](5-methylfuran-2-yl)methanone; [3-(5-methylfuran-2-carbonyl) 1-phenyl-4,5-dihydro-1H-pyrazol-5-yl](2-nitrophenyl)methanone against P. falciparum. Based upon our findings, it is concluded that the molecular scaffold of 7[5-(2-chlorobenzoyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl](5 methylfuran-2-yl)methanone; [3-(5-methylfuran-2-carbonyl)-1-phenyl-4,5 dihydro-1H-pyrazol-5-yl](2-nitrophenyl)methanone may be used as a lead structure for further modifications in the search of more potent antimalarial drug molecules.

**KEYWORDS:** Heterocyclic compound, five membered, Pyrazole; Pyrazoline; Synthesis

## Introduction

Malaria is a life-threatening disease spread to humans by some types of mosquitoes. It is mostly found in tropical countries. It is preventable and curable. The infection is caused by a parasite and does not spread from person to person. Symptoms can be mild or life-threatening. Mild symptoms are fever, chills and headache. Severe symptoms include fatigue, confusion, seizures, and difficulty breathing.Infants, children under 5 years, pregnant women and girls, travellers and people with HIV or AIDS are at higher risk of severe infection. Malaria can be prevented by avoiding mosquito bites and with medicines. Treatments can stop mild cases from getting worse. Malaria mostly spreads to people through the bites of some infected female *Anopheles* mosquitoes. Blood transfusion and contaminated needles may also transmit malaria. The first symptoms may be mild, similar to many febrile illnesses, and difficulty to recognize as malaria. Left untreated, *P. falciparum* malaria can progress to severe illness and death within 24 hours.

There are 5 *Plasmodium* parasite species that cause malaria in humans and 2 of these species – *P. falciparum* and *P. vivax* – pose the greatest threat. *P. falciparum* is the deadliest malaria parasite and the most prevalent on the African continent. *P. vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa. The other malaria species which can infect humans are *P. malariae, P. ovale* and *P. knowlesi*.

According to the latest World malaria report, there were 263 million cases of malaria in 2023 compared to 252 million cases in 2022. The estimated number of malaria deaths stood at 597 000 in 2023 compared to 600 000 in 2022.The WHO African Region continues to carry a disproportionately high share of the global malaria burden. In 2023 the Region was home to about 94% of all malaria cases and 95% of deaths. Children under 5 years of age accounted for about 76% of all malaria deaths in the Region.Over half of these deaths occurred in four countries: Nigeria (30.9%), the Democratic Republic of the Congo (11.3%), Niger (5.9%) and United Republic of Tanzania (4.3%). Symptoms may be mild for some people, especially for those who have had a malaria infection before. Because some malaria symptoms are not specific, getting tested early is important. Some types of malaria can cause severe illness and death. Infants, children under 5 years, pregnant women, travellers and people with HIV or AIDS are at higher risk. Severe symptoms include: extreme tiredness and fatigue, impaired consciousness, multiple convulsions, difficulty breathing, dark or bloody urine, jaundice (yellowing of the eyes and skin), abnormal bleeding.

People with severe symptoms should get emergency care right away. Getting treatment early for mild malaria can stop the infection from becoming severe. Malaria infection during pregnancy can also cause premature delivery or delivery of a baby with low birth weight. Malaria can be prevented by avoiding mosquito bites and by taking medicines. Talk to a doctor about taking medicines such as chemoprophylaxis before travelling to areas where malaria is common.

### Vector control

Vector control is a vital component of malaria control and elimination strategies as it is highly effective in preventing infection and reducing disease transmission. The 2 core interventions are insecticide-treated nets (ITNs) and indoor residual spraying (IRS). Progress in global malaria control is threatened by emerging resistance to insecticides among *Anopheles* mosquitoes. However, new generation nets, which provide better protection against malaria than pyrethroid-only nets, are becoming more widely available and represent an important tool in global efforts to combat malaria.

*Anopheles stephensi* presents an added challenge for malaria control in Africa. Originally native to parts of south Asia and the Arabian Peninsula, the invasive mosquito species has been expanding its range over the last decade, with detections reported to date in eight African countries. *An. stephensi* thrives in urban settings, endures high temperatures and is resistant to many of the insecticides used in public health.

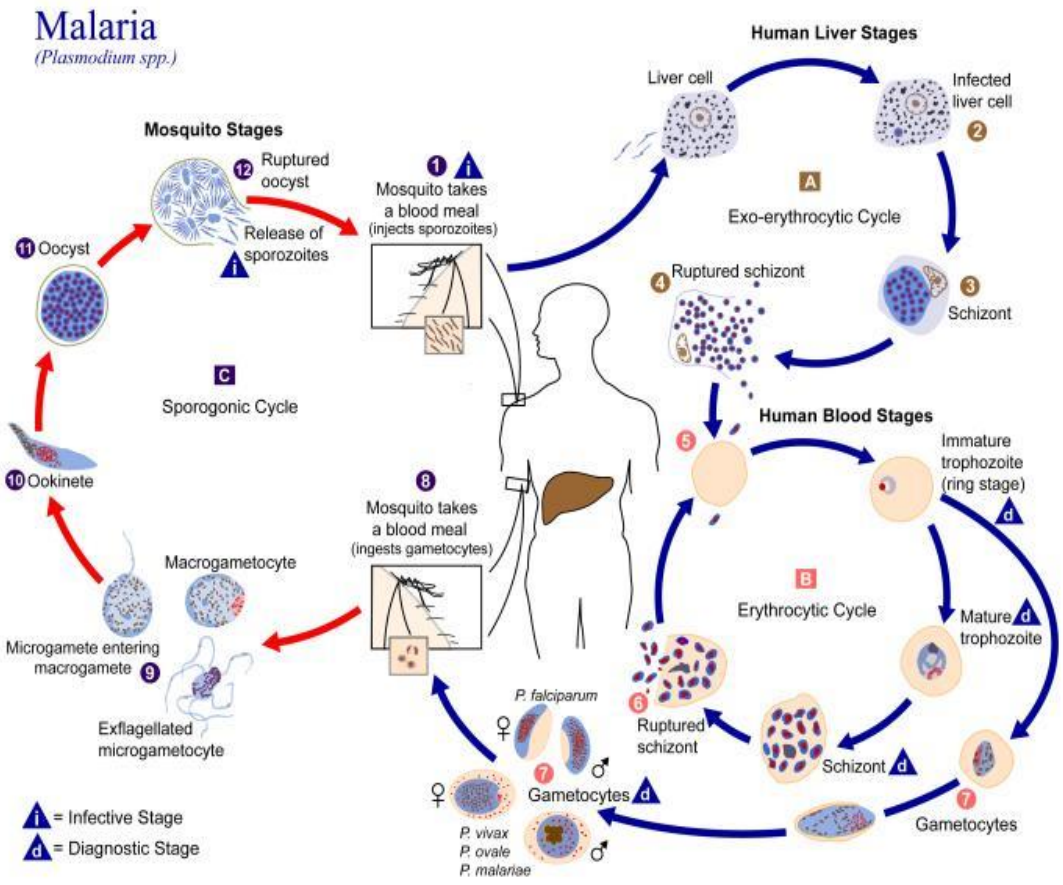



**Figure 1.2: Parasite life cycle**

### Chemoprophylaxis

Travellers to malaria endemic areas should consult their doctor several weeks before departure. The medical professional will determine which chemoprophylaxis drugs are appropriate for the country of destination. In some cases, chemoprophylaxis drugs must be started 2–3 weeks before departure. All prophylactic drugs should be taken on schedule for the duration of the

stay in the malaria risk area and should be continued for 4 weeks after the last possible exposure to infection since parasites may still emerge from the liver during this period.

**Preventive chemotherapies**

Preventive chemotherapy is the use of medicines, either alone or in combination, to prevent malaria infections and their consequences. It requires giving a full treatment course of an antimalarial medicine to vulnerable populations at designated time points during the period of greatest malarial risk, regardless of whether the recipients are infected with malaria.

Preventive chemotherapy includes perennial malaria chemoprevention (PMC), seasonal malaria chemoprevention (SMC), intermittent preventive treatment of malaria in pregnancy (IPTp) and school-aged children (IPTsc), post-discharge malaria chemoprevention (PDMC) and mass drug administration (MDA). These safe and cost-effective strategies are intended to complement ongoing malaria control activities, including vector control measures, prompt diagnosis of suspected malaria, and treatment of confirmed cases with antimalarial medicines.

**Vaccine**

Since October 2021, WHO has recommended broad use of the RTS,S/AS01 malaria vaccine among children living in regions with moderate to high *P. falciparum* malaria transmission. The vaccine has been shown to significantly reduce malaria, and deadly severe malaria, among young children. In October 2023, WHO recommended a second safe and effective malaria vaccine, R21/Matrix-M. Vaccines are now being rolled out in routine childhood immunization programmes across Africa. Malaria vaccines in Africa are expected to save tens of thousands of young lives every year. The highest impact will be achieved, however, when the vaccines are introduced alongside a mix of other WHO-recommended malaria interventions such as bed nets and chemoprophylaxis.

**PYRAZOLINES:**

Heterocyclic compounds are carbocyclic compounds in which one or more carbon atoms have been substituted by other atoms. Natural substances with heterocyclic ring systems include autacoids, antibiotics, haemoglobin, hormones, alkaloids, vitamins, and chlorophyll. Synthetic substances with heterocyclic ring systems include pharmaceuticals and colours. This makes it essential to investigate heterocyclic molecules.

The most prevalent substitutes for carbon are oxygen, nitrogen, and sulphur, with nitrogen containing heterocycles such as pyrimidine, pyridazine, piperazine, pyrazole, and pyrrole being the most common. For five-membered rings with nitrogen as a hetero element, the azole suffix is used.

Pyrazole is a compound made up of a five-membered, doubly unsaturated ring with two neighbouring nitrogen atoms (Figure 1.3).

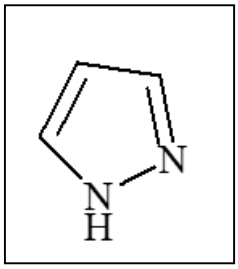
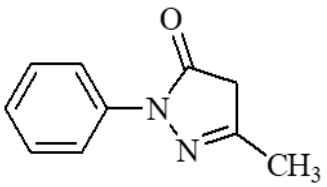



**Figure 1.3: Pyrazole**

L-phenyl-3-methyl-5-pyrazolone (Figure 1.4) was created by Knorr in 1883 using phenyl hydrazine and ethyl acetoacetate. This is the first instance of a synthetic chemical with this mechanism that has been documented. In order to indicate that the molecule was created by swapping out one of the carbons in pyrrole with nitrogen (22), Knorr gave it the name "pyrazole."




## MATERIALS AND METHODS

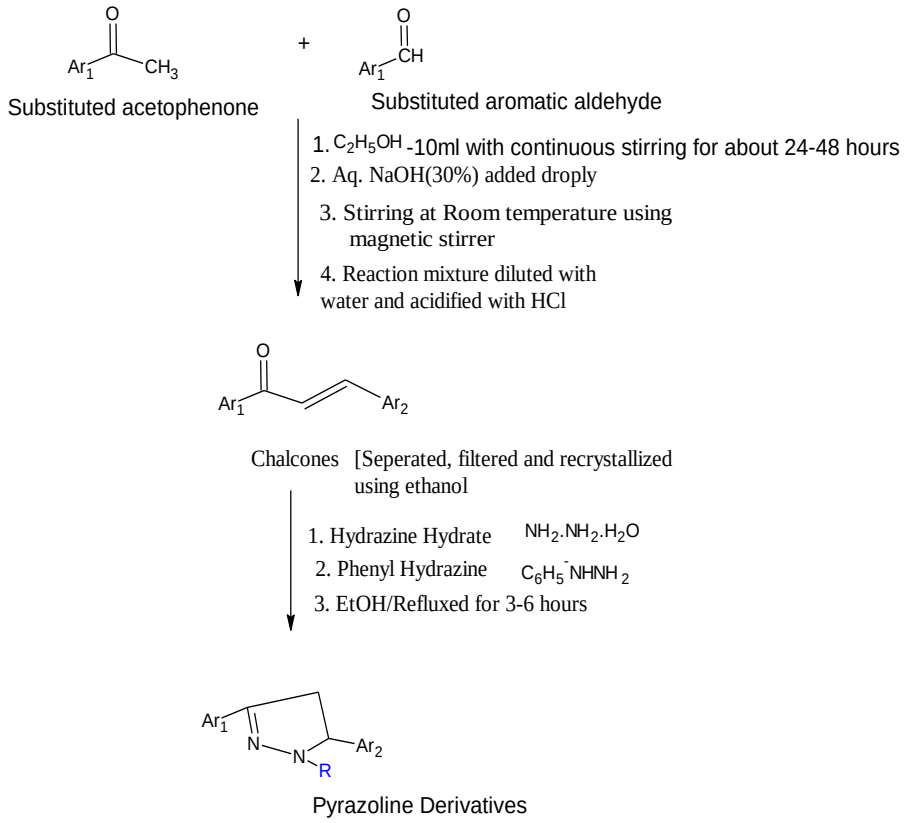
### MATERIALS:

The “reagents/chemicals/solvents used during the course of the studies were procured from different chemical units- Merck (India), Qualigens, SD Fine, SRL and CDH and used without” purification. “Purity of the compounds was checked by TLC, performed with silica gel 60 F254 (Merck) and the spots were located either under ultra violet light or through exposure to iodine vapours”.

The following solvent systems were used for TLC:

- Solvent System I- Methanol: Chloroform (2:8)
- Solvent System II- Benzene: Acetone (7:3)
- Whatman filter paper (No. 1) was used for filtration.

## Scheme




## List of compounds synthesized

| Derivatives | $Ar_1$ | $Ar_2$ | R |
|---|---|---|---|
| **1a** | $C_6H_5NH_2$ | 4-Pyridine carboxyldehyde | Hydrazine |
| **1b** | $C_6H_5NH_2$ | 2-Chloro benzaldehyde | Hydrazine |
| **1c** | $C_6H_5NH_2$ | 2-Nitrobenzaldehyde | Hydrazine |
| **1d** | $C_6H_5NH_2$ | 4-Pyridine carboxyldehyde | Phenyl Hydrazine |
| **1e** | $C_6H_5NH_2$ | 2-Chloro benzaldehyde | Phenyl Hydrazine |
| **1f** | $C_6H_5NH_2$ | 2-Nitrobenzaldehyde | Phenyl Hydrazine |
| **2a** | $C_6H_5COCH_3$ | 4-Pyridine carboxyldehyde | Hydrazine |
| **2b** | $C_6H_5COCH_3$ | 2-Chloro benzaldehyde | Hydrazine |
| **2c** | $C_6H_5COCH_3$ | 2-Nitrobenzaldehyde | Hydrazine |

| | | | |
|---|---|---|---|
| **2d** | $C_6H_5COCH_3$ | 4-Pyridine carboxyldehyde | Phenyl Hydrazine |
| **2e** | $C_6H_5COCH_3$ | 2-Chloro benzaldehyde | Phenyl Hydrazine |
| **2f** | $C_6H_5COCH_3$ | 2-Nitrobenzaldehyde | Phenyl Hydrazine |
| **3a** | 5-MethylFurfuryl | 4-Pyridine carboxyldehyde | Hydrazine |
| **3b** | 5-MethylFurfuryl | 2-Chloro benzaldehyde | Hydrazine |
| **3c** | 5-MethylFurfuryl | 2-Nitrobenzaldehyde | Hydrazine |
| **3d** | 5-MethylFurfuryl | 4-Pyridine carboxyldehyde | Phenyl Hydrazine |
| **3e** | 5-MethylFurfuryl | 2-Chloro benzaldehyde | Phenyl Hydrazine |
| **3f** | 5-MethylFurfuryl | 2-Nitrobenzaldehyde | Phenyl Hydrazine |

**PROCEDURE:**

**Step-1. Synthesis of chalcones:**

Equimolar "quantity of substituted acetophenone (0.01 mol) and substituted aldehyde (0.01 mol) was dissolved in ethanol (l0ml) under stirring & aq NaOH (30 %) was added dropwise; the reaction mixture stirred at room temperature using magnetic stirrer & kept for few hour and the reaction mixture was diluted with water & acidified with HCl; the separated solid was filtered and recrystallised from" ethanol.

**Step-2. Synthesis of pyrazoline derivatives:**

"A mixture of chalcones (0.01 mol), 2,4-dinitrophenyl hydrazine reagent dissolved in ethanol; the resulting mixture was refluxed for 2 or 3 hours and the resulting mixture was poured into ice water". The separated solid were filtered and recrystallised from ethanol.

**[3-(4-aminophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl](2-chlorophenyl) methanone (3a)** FTIR, 3120.76 Aromatic C-H, stretching, 1692.8-C=O, 1628.10-C=N, 1531.58-N=N, 1163.11-Aryl NH2, 951.92-N-N, 733.32-Aromatic C-H, bending. **NMR spectra,** 6-88 Ar-H aromatic, 0.875 Triplet, Primary R-CH3, 1.325 Singlet, R2-CH2, 1.498 Tertiary, R3-CH, 1.721 Allylic –C=C-C-H.

**[3-(4-aminophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl](2-nitrophenyl)methanone (3b) FTIR Spectra** 2903.67 Aromatic C-H, stretching, 1641.09C=N, 1546.91 N=N, 1313.05 Aryl $NH_2$, 1055.32 N-N, 899.82 Aryl C-Cl stretching, 814.33 "Aromatic C-H, bending. **1H-NMR Spectra** 6-88 Ar-H aromatic, 0.875 Triplet, Primary R-CH3, 1.325 Singlet, R2-CH2, 1.498 Tertiary, R3-CH, 1.721 Allylic –C=C-C-H

**1-{4-[5-(pyridine-4-carbonyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl}ethan-1-one"(3c) FTIR Spectra** 2923.67 Aromatic C-H, stretching, 1611.09 C=N, 1526.91 N=N, 1311.05 Aryl $NH_2$, 1054.32 N-N, 889.82 Aryl C-Cl stretching, 814.33 "Aromatic C-H, bending. **1H-NMR Spectra** 6-81 Ar-H aromatic, 0.87 Triplet, Primary R-CH3, 1.35 Singlet, R2-CH2, 1.48 Tertiary, R3-CH, 1.721 Allylic –C=C-C-H

**1-{4-[1-phenyl-5-(pyridine-4-carbonyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl}ethan-1-one"(3d) FTIR Spectra** 2903.67 Aromatic C-H, stretching, 1641.01 C=N, 1516.91N=N, 1311.05 Aryl $NH_2$, 1051.32 N-N, 891.82 Aryl C-Cl stretching, 814.31 "Aromatic C-H, bending. **1H-NMR Spectra** 6-81 Ar-H aromatic, 0.87 Triplet, Primary R-CH3, 1.32 Singlet, R2-CH2, 1.418 Tertiary, R3-CH, 1.71 Allylic –C=C-C-H.

**[3-(4-aminophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl](2-chlorophenyl) methanone (3e)** FTIR, 3120.76 Aromatic C-H, stretching, 1692.8-C=O, 1628.10-C=N, 1531.58-N=N, 1163.11-Aryl NH2, 951.92-N-N, 733.32-Aromatic C-H, bending. **NMR spectra,** 6-88 Ar-H aromatic, 0.875 Triplet, Primary R-CH3, 1.325 Singlet, R2-CH2, 1.498 Tertiary, R3-CH, 1.721 Allylic –C=C-C-H.

**[3-(4-aminophenyl)-4,5-dihydro-1*H*-pyrazol-5-yl](2-nitrophenyl)methanone (3f) FTIR Spectra** 2903.67 Aromatic C-H, stretching, 1641.09C=N, 1546.91 N=N, 1313.05 Aryl $NH_2$, 1055.32 N-N, 899.82 Aryl C-Cl stretching, 814.33 "Aromatic C-H, bending. **1H-NMR Spectra** 6-88 Ar-H aromatic, 0.875 Triplet, Primary R-CH3, 1.325 Singlet, R2-CH2, 1.498 Tertiary, R3-CH, 1.721 Allylic –C=C-C-H

**Analytical data of isolated compound**

| Derivatives | Chemical Formula | M.W | Composition | | | | | M.P.(°C) |
|---|---|---|---|---|---|---|---|---|
| | | | C | H | Cl | N | O | |
| **1a** | $C_{15}H_{12}N_4O$ | 264.28 | 68.17% | 4.58% | --- | 21.20% | 6.05% | 214.99°C |
| **1b** | $C_{16}H_{14}N_3OCl$ | 299.75 | 64.11% | 4.71% | 11.83% | 14.02% | 5.3% | 257.90°C |
| **1c** | $C_{16}H_{14}N_4O_3$ | 310.30 | 61.93% | 4.55% | --- | 18.065 | 15.475 | 296.10°C |
| **1d** | $C_{21}H_{18}N_4O$ | 342.39 | 73.67% | 5.30% | --- | 16.36% | 4.67% | 235.51°C |
| **1e** | $C_{22}H_{18}N_3OCl$ | 375.85 | 70.30% | 4.83% | 9.43% | 11.18% | 4.26% | 205.17°C |
| **1f** | $C_{22}H_{18}N_4O_3$ | 386.40 | 68.38% | 4.70% | --- | 14.50% | 12.42% | 232.98°C |
| **2a** | $C_{17}H_{15}N_3O_2$ | 293.31 | 69.61% | 5.15% | --- | 14.33% | 10.91% | 190.47°C |
| **2b** | $C_{18}H_{15}N_2O_2Cl$ | 326.77 | 66.16% | 4.63% | 10.85 | 8.57% | 9.79% | 197.20°C |
| **2c** | $C_{18}H_{15}N_3O_4$ | 337.32 | 64.09% | 4.48% | --- | 12.46% | 18.97% | 245.70°C |
| **2d** | $C_{23}H_{19}N_3O_2$ | 369.41 | 74.78% | 5.18% | --- | 11.37% | 8.66% | 215.71°C |
| **2e** | $C_{24}H_{19}N_2O_2Cl$ | 402.87% | 71.55% | 4.75% | 8.80% | 6.95% | 7.94% | 250.47°C |
| **2f** | $C_{24}H_{19}N_3O_4$ | 413.04% | 69.72% | 4.63% | --- | 10.16% | 15.48% | 294.59°C |
| **3a** | $C_{18}H_{15}N_3O_4$ | 283.28 | 63.60% | 4.63% | --- | 14.83% | 16.94% | 245.70°C |
| **3b** | $C_{16}H_{13}N_2O_3Cl$ | 316.73 | 60.67% | 4.14% | 11.19% | 8.84% | 15.1% | 221.96°C |
| **3c** | $C_{16}H_{13}N_3O_5$ | 327.29 | 58.72% | 4.00% | --- | 12.84% | 24.44% | 207.69°C |
| **3d** | $C_{21}H_{17}N_3O_3$ | 359.37 | 70.18% | 4.77% | --- | 11.69% | 13.36% | 214.13°C |
| **3e** | $C_{22}H_{17}N_2O_3Cl$ | 392.83 | 67.26% | 4..36% | 9.02% | 7.13% | 12.22 | 253.17°C |
| **3f** | $C_{22}H_{17}N_3O_5$ | 403.38 | 65.50% | 4.25% | --- | 10.42% | 19.83% | 116.00°C |

## CULTIVATION OF MALARIA PARASITES

### Medium preparation for cultivation of malaria:

In 960 mL of triple-distilled water, one package of RPMI 1640 was dissolved, and 2 mg of glucose was added. To stop contamination, gentamycin sulphate (40 µg/mL) was added. By running the solution through a millipore filter with a 0.22 µm porosity, the solution was sterilised. 96 mL aliquots of this were kept at 4 °C in a glass media bottle.

## IN VITRO ANTIMALARIAL DETERMINATION (83)

It was done by Schizont maturation inhibition (SMI) assay, and involved the following steps:

- Stock solutions of the synthesised compounds (1 mg/mL) were prepared by dissolving in 100 µL DMSO and 900 µL incomplete media.
- RPMI 1640 medium was used to dilute this to acquire various medication concentrations. These dilutions were applied to 96-well microplates with flat bottoms.
- Only culture media was present in the negative control wells.
- Synchronised cultures with a final haematocrit of 5% and parasiternia of 1% were aliquoted into the plates, where they were then incubated at 37°C.
- After 24 to 30 hours of culture, growth was observed.
- After schizont maturation was confirmed, blood smears were made from each well.
- All slides were stained with Giemsa/JSB I and JSB II after being fixed in methanol.
- 200 asexual stage parasites were used as a proxy for the number of schizonts. The values from the test wells and the control wells were compared.
- Using HN-NonLin V l.1, the IC50 of each chemical was then calculated.
- The standard drug used was chloroquine.

The $IC_{50}$ values and % inhibition of compounds of the series are presented in Table 3.4 respectively.

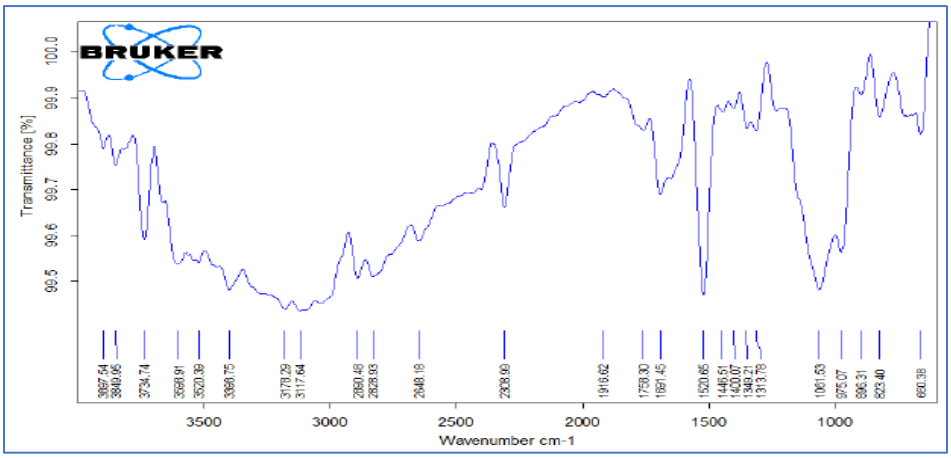
**Table** 3.**4: *In vitro* antimalarial activity and cytotoxicity of pyrazoline derivatives**

| **Compound No** | **Concentration** | **No. of Schizonts/200parasites** | **% inhibition** | **$IC_{50}$** | | **SI** |
|---|---|---|---|---|---|---|
| | | | | **µg/mL** | **µM** | |
| **1b** | Control | 125 | 100 | 17.54 | 39.20 | ND |
| | 1.9 | 119 | 91 | | | |
| | 4.2 | 115 | 87 | | | |
| | 8.2 | 116 | 76 | | | |
| | 16.3 | 82 | 53 | | | |
| | 32.5 | 54 | 26 | | | |
| | 65 | 5 | 04 | | | |
| | 125 | 0 | 0 | | | |
| **1c** | Control | 130 | 100 | 18.82 | 39.41 | ND |
| | 1.9 | 125 | 92 | | | |
| | 4.2 | 116 | 85 | | | |
| | 8.2 | 102 | 79 | | | |
| | 16.3 | 79 | 55 | | | |

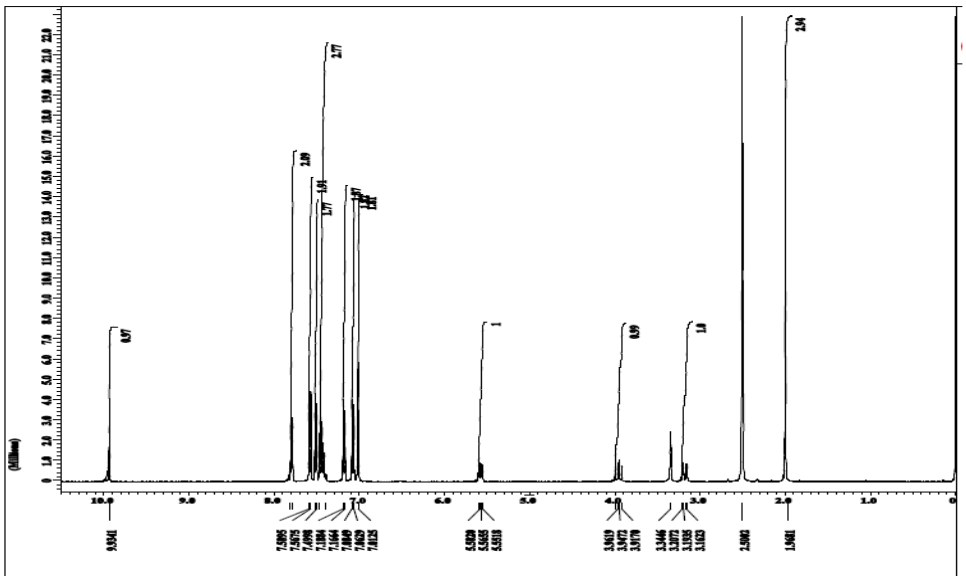
| | | | | | | |
|---|---|---|---|---|---|---|
| | 32.5 | 36 | 21 | | | |
| | 65 | 0 | 0 | | | |
| | 125 | 0 | 0 | | | |
| **2a** | Control | 133 | 100 | 25.52 | 50.28 | ND |
| | 1.9 | 128 | 95 | | | |
| | 4.2 | 125 | 90 | | | |
| | 8.2 | 116 | 81 | | | |
| | 16.3 | 89 | 66 | | | |
| | 32.5 | 52 | 35 | | | |
| | 65 | 0 | 0 | | | |
| | 125 | 0 | 0 | | | |
| **2d** | Control | 135 | 100 | 29.95 | 69.41 | ND |
| | 1.9 | 129 | 97 | | | |
| | 4.2 | 123 | 93 | | | |
| | 8.2 | 117 | 87 | | | |
| | 16.3 | 99 | 74 | | | |
| | 32.5 | 64 | 48 | | | |
| | 65 | 0 | 0 | | | |
| | 125 | 0 | 0 | | | |
| **3e** | Control | 130 | 100 | 32.02 | 71.24 | ND |
| | 1.9 | 125 | 97 | | | |
| | 4.2 | 121 | 94 | | | |
| | 8.2 | 106 | 86 | | | |
| | 16.3 | 97 | 72 | | | |
| | 32.5 | 71 | 52 | | | |
| | 65 | 0 | 0 | | | |
| | 125 | 0 | 0 | | | |
| **3f** | Control | 131 | 100 | 0.90 | 1.63 | 47 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 1.9 | 123 | 75 | | | |
| | 4.2 | 67 | 45 | | | |
| | 8.2 | 0 | 0 | | | |
| | 16.3 | 0 | 0 | | | |
| | 32.5 | 0 | 0 | | | |
| | 65 | 0 | 0 | | | |
| | 125 | 0 | 0 | | | |
| **Chloroquine** | - | - | - | 0.002 | - | - |

**FTIR and NMR Spectra of potent compound.**




**FTIR Spectra of 1-{4-[1-phenyl-5-(pyridine-4-carbonyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl}ethan-1-one"**



**1H-NMR Spectra of compound 1-{4-[1-phenyl-5-(pyridine-4-carbonyl)-4,5-dihydro-1*H*-pyrazol-3-yl]phenyl}ethan-1-one"**

## RESULTS AND CONCLUSION

Over a million people die from malaria each year, a terrible disease brought on by several Plasmodium parasite species. Due to the emergence of resistance, efforts to eradicate the disease with the arsenal of agents have been shown to be fruitless. As a result, the quest for medications to cure malaria is ongoing. Pyrazoline appears to be a successful heterocyclic in this regard. Hybrid technology, wherein many moieties are covalently connected to one another, is the newest approach in malaria treatment. Pyrazoline was combined with other bioactive components based on the idea that their coexistence in a single molecular framework might greatly increase the biological activity of the resulting molecules. This approach took into account pyrazoline's pharmacological importance.

The several sets of synthesised pyrazoline-based compounds include 1b, lc, 2a, 2d, 3e, and 3f. 18 different compounds were created in this series. The purity of the compounds was verified using TLC and melting point. The characterising C, H, and N studies of the synthesised compounds revealed values that were within the acceptable ranges of 0.4 of theoretical values. The true structures were further confirmed by IR and NMR spectroscopy. The three protons of the pyrazoline ring, HA, HM, and HX, appeared as doublets of doublets in the lH-NMR's characteristic AMX pattern, which is how pyrrazolines were distinguished from other compounds. Due to its cisoid connection to the HX proton and geminally to the HM proton, the HA proton appeared as a doublet of doublet at about 8:3.25. The HM proton, deshielded to some extent by aryl group appeared around 8 3.75 and was coupled transoid to HX proton and gerninally to HA proton. "The HX proton also gave doublet of doublet around 8 5.75, it was more deshielded due to effect of aryl group and electronegative nitrogen and was coupled transoid to the HM proton and cisoid to the HA proton".

Once characterised the compounds were evaluated for in vitro antimalarial activity by MMT assay, using chloroquine sensitive 3D7 strain. "The compounds with $IC_{50}$ less than 5 μM were further evaluated for their cytotoxicity effect by Mosmann method".

The series' title compounds were initially created via synthesising hydrazines. But there were no positive in vitro outcomes. A second set of INH derivatives were created in order to boost the hydrophobicity of the series. However, even with this set, no useful findings were attained. As a result, cytotoxicity tests for the compounds in this series were not conducted. The falcipain enzyme did not interact favourably with any positions, not even docked poses.

Compounds from the sequence la, 1d, le, le, 2b, 2c, 2e, 2f, 3a, 3b, 3c, and 3d, however, were unable to exhibit significant antimalarial activity.

Overall, 3e and 3f exhibit significant antimalarial action. Further in silico research is being done to create additional effective agents using these two compounds as templates, and then the synthesis of those compounds will be done.

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