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SYNTHESIS, CHARACTERIZATION, DOCKING STUDY AND BIOLOGICAL EVALUATION OF NEW CHALCONE, PYRAZOLINE, AND PYRIMIDINE DERIVATIVES AS POTENT ANTIMALARIAL COMPOUNDS

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ABSTRACT:

In this investigation, pyrimidine derivatives were produced by reacting one mole of cyanoguanidine with one mole of gluconate derivatives in ethanol as the solvent. This reaction was carried out successfully. As a consequence, heterocyclic hexagonal rings were produced. Spectroscopic measurements, such as infrared spectra, proton nuclear magnetic resonance spectra, and carbon-13 nuclear resonance spectra, in addition to measurements of physical properties, such as colour, molecular weight, and melting point, were utilised to validate the correctness of the compositions of the compounds that were prepared. Staphylococcus aureus, a Gram-positive bacterium, and Escherichia coli, a Gram-negative bacteria, were the two types of hazardous bacteria that were taken into consideration by the researchers as they investigated the impacts of a few different compounds. Dimethyl sulfoxide (DMSO) solutions with concentrations of 0.01, 0.001, and 0.0001 mg/ml were used to dissolve both medicines (I9 and I16) in a Multer Hinton Agar growth medium. The concentrations of the DMSO solutions were different. In the study, the sensitivity of the bacterial isolates was investigated via the use of the diffusion method. The antibiotic Ciprofloxacin was employed as the control sample. A number of different dosages of compound I15 were used to study its effect on the elimination of free radicals. DPPH root was also used.

Keywords: *synthesis, biological evaluation, pyrimidine derivatives.*

Introduction:

Amoebiasis, which is the protozoal infection that is the most lethal, is also one of the top two or three parasitic illnesses in terms of having the highest fatality rate. Entamoeba histolytica, a protozoan parasite, is directly responsible for the development of amoebiasis and amoebic dysentery. Despite the fact that it

may be discovered worldwide, this parasite is often more prevalent in tropical and subtropical regions. It has been shown that metronidazole may induce cancer in rats and mutations in microbes, despite the fact that it is the medication of choice for treating amoebiasis owing to its outstanding effectiveness as an amoebicide. When used regularly to treat infections caused by E. histolytica, common antiamoebic medications have a greater risk for harm and may lead to clinical resistance. In light of this, there is an urgent need for innovative amoebiasis therapies that are less harmful and more effective. Significant biological effects may be attributed to five-membered heterocyclic molecules, whether they are created chemically or arise naturally. molecules that include a pyrimidine ring are of high interest in the field of biological sciences due to the versatility of these molecules. Because of these discoveries, we decided to proceed with our program of generating heterocycles with the purpose of using them as antiamoebic medicines. Towards this purpose, we have synthesised a novel class of chemical compounds that contain two pyrimidine rings and tested them against the protozoan HM1: IMSS strain of E. histolytica, which is the agent that causes amoebiasis. Because of their activity and favourable therapeutic indices, these compounds were selected as potential study topics because of their potential for use.

Chemistry

Different substituted aromatic acetophenones (a-h) were reacted with teraphthaldi carboxaldehyde in NaOH and methanol to produce the corresponding bis-chalcones 2a-2h, which were then used to synthesise the 2,4,6-trisubstituted bis-pyrimidine derivatives (3a-3h and 4a-4h). Scheme1. The hydrochloride salts of pyrrolidine and piperidine were prepared by refluxing the corresponding anhydrides with S-methyl isothiourea sulphate in water, as detailed in the aforementioned method.

Pharmacology

Microdilution was used to perform in vitro screening against the HM1: IMSS strain of E. histolytica for all newly synthesised bis-pyrimidine derivatives (3a-3h) and (4a-4h). The screening was carried out against the yeast strain. The tests were carried out three times for each dosage level for each individual. In order to examine the cytotoxicity of active compounds, researchers have used the MTT test on the PC12-rat pheochoromocytoma cell line.

Synthesis

The synthesis of the 2,4,6-trisubstituted bis-pyrimidine derivatives (3a-3h and 4a-4h) was carried out by following the processes that are outlined in Scheme 1. As shown by the existence of distinct bands at 1650-1661 cm−1 and 1572-1589 cm−1 in the infrared spectra of bis-chalcones (2a-2h), which correspond to the

α and β unsaturated carbonyl groups and C=C, respectively, it was determined that the terephthaldicarboxaldehyde underwent condensation with substituted acetophenones. Because of the emergence and spread of parasites that are resistant to the majority of the antimalarial drugs and drug combinations that are now in use, as well as the lack of a real malaria vaccine, there is an increased need for the development of novel therapies in order to address this global problem. The ability of a parasite strain to survive and/or reproduce when it is treated with medicine at doses that are equivalent to or more than what is generally given is referred to as antimalarial drug resistance.

Antimalarial drug

Malaria parasites are able to develop resistance mechanisms as a result of the massive and reckless use of antimalarial drugs such as chloroquine and artemisinin. This creation of resistance mechanisms presents a significant challenge for attempts to control malaria. Because of this, there is an urgent need for the creation of innovative antimalarial medications that may be used for therapeutic purposes. As a result of the better biological friendliness of natural products, antimalarial drugs that make use of a natural product scaffold have been examined for their potential use in the synthesis of target molecules. The roots of a large number of small molecule drugs that are now available may be traced back to scaffolds that are generated from natural sources. These scaffolds may be perfect for the creation of new antimalarials. Nevertheless, the natural lead compounds that are formed from these scaffolds present a number of problems that need to be solved before they can be used. A restricted solubility in water, mechanical or chemical instability, and a wide spectrum of biological consequences are some of the factors that fall into this category.

OBJECTIVE:

- To study on synthesis, characterization
- To study on biological evaluation of pyrimidine derivatives

RESEARCH MYTHOLOGY

The parasite Plasmodium, which is responsible for malaria, is spread from one person to another by the bite of a mosquito vector. When it comes to tropical parasite illnesses, malaria is one of the most destructive and prevalent diseases that can be found in underdeveloped nations. There were around 229 million cases of malaria in 2019, according to the World Health Organisation (WHO), which reported that there were 87 countries that were considered to be malaria endemic. Malaria is a persistent danger to around fifty percent of the world's population, according to the Organisation for Economic Cooperation and Development

(2020). Plasmodium falciparum, Plasmodium vivax, Plasmodium ovalae, Plasmodium malariae, and Plasmodium knowelsi are the five types of plasmodium that are usually recognised to infect people. The parasite P. falciparum, on the other hand, is responsible for the greatest incidence of complications and fatality. The parasites enter the human body by the bite of an infected mosquito, which then travels through the circulation, multiplies in the cells of the liver, and then is released back into the bloodstream. Once there, the parasites swiftly reorganise themselves by inserting their proteins, infecting and destroying the red blood cells. There are two hosts involved in the life cycle of the malaria parasite. A female Anopheles mosquito that is infected with malaria injects sporozoites into a human host while the insect is feeding on another person's blood. Infecting liver cells, sporozoites eventually develop into schizonts, which then burst and release merozoites throughout the process.

Plasmodium falciparum, the intraerythrocytic malaria parasite, is responsible for maintaining a low cytosolic Na (+) content. The plasma membrane P-type cation translocating ATPase, also known as PfATP40, has been shown to play a significant part in this process. PfATP4 has been the focus of a significant amount of attention in recent years due to the fact that mutations in this protein confer resistance to an increasing number of new antimalarial compounds. These compounds include the spiroindolones, the pyrazoles, the dihydroisoquinolones, and a number of the antimalarial agents that are included in the "Malaria Box" that is distributed by Medicines for Malaria Venture. According to Spillman et al. (2013), when parasites are exposed to these chemicals, there is a severe disturbance of the cytosolic sodium (Na+) concentration. It is not yet known whether or whether such chemically unique chemicals interact with PfATP4, and if they do, how they do so. Additionally, it is not yet evident how such interactions lead to the death of the parasite. The relevance of PfATP4 as a potential target for next generation antimalarial drugs is shown by the fact that it has been focused upon by a number of distinct chemical classes. The spiroindolone, which was formerly known as KAE609 and is now known as cipargamin, has made significant progress in Phase I and IIa clinical studies, earning positive results. This study takes into consideration the physiological function that PfATP4 plays, provides a summary of the present repertory of antimalarial drugs for which PfATP4 is implicated in their mechanism of action, and offers a perspective on the translation of target identification in the laboratory to patient therapy in the field.

As a result of the absence of a reliable malaria vaccine, as well as the appearance and dissemination of parasites that are resistant to the majority of the antimalarial medications and drug combinations that are currently being used in clinical settings, there is an urgent need to find new treatments that are effective against malaria. The capacity of a parasite strain to live and/or reproduce in spite of the administration of medication in dosages that are equivalent to or greater than those that are typically suggested is what is

referred to as antimalarial drug resistance. The widespread and indiscriminate use of antimalarial medications like chloroquine and artemisinin leads to the evolution of resistance mechanisms in malaria parasites, which is a serious danger to the control of malaria. Antimalarial drug resistance is a major challenge to the control of malaria. For this reason, the development of novel antimalarial drugs is essential for the provision of effective treatment. As a result of the fact that natural products are less harmful to living organisms, antimalarial medicines that include natural product scaffold have been investigated in the process of developing target molecules.

Natural-based scaffolds, which may be regarded to be preferred structures for the identification of novel antimalarials, were used in the development of a significant number of small molecule medications that are now available on the market. However, there are a few challenges that are linked with the natural lead compounds that are formed from these scaffolds. These challenges include their synthesis, limited aqueous solubility, chemical or metabolic instability, and a broad range of biological effects. These challenges need to be solved. With regard to the comprehensive therapy of malaria and the problem of resistance, these antimalarial drugs will continue to be in high demand by the medical community.

Fig. 1. Structures of chalcone, pyrazoline and pyrimidine.

A chloroquine-resistant strain of Plasmodium falciparum known as RKL9 and a reference strain known as 3D7 were used in order to evaluate the effectiveness of the chemicals that were synthesised in terms of their ability to inhibit the growth of malaria parasites. For the purpose of comparing the IC50 and IC80 values of the compounds that were created, the benchmarks that were used were chloroquine diphosphate (CQ) and artemisinin (Artemisinin). This information is summarised in Table 1, which can be found here. To determine whether or not any of the compounds (1-4, 1Ai-iii-4Ai-iii, 1Bi-ii 4Bi-ii) that were synthesised in this study has antimalarial properties, they were tested against P. falciparum. When compared to the compounds that served as the reference, the majority of the compounds showed findings that were encouraging. The most active molecule among all of those that were investigated was found to be 1Aiii, which had an IC50 value of 2.1 lg/mL, an IC80 value of 8 lg/mL, and an IC50RKL9 value of 1.1 lg/mL (Table 1). Depending on whether or not carbothioamide functionality is present, compounds 2Aiii, 3Aiii, and 4Aiii exhibit distinct reactions. A comparison was made between the antimalarial activity of chalcones

1, 2, and 4 and that of heterocyclic compounds generated from these chalcones. The heterocyclic compounds were shown to be more effective against Plasmodium falciparum. Furthermore, as can be seen in Figure 2, compounds that included a methoxy group in the para position demonstrated a higher level of activity in comparison to compounds that had a methoxy group in the meta position.

Molecular docking

In this study, we investigated the behaviour of each of the synthesised compounds. It is necessary for a chemical to possess the appropriate proportion of hydrophilic and hydrophobic properties in order for it to go past the cell membrane and enter the circulation. This is necessary for the chemical to be considered a good medication. The degree to which a molecule is able to dissolve in water is directly proportional to the number of hydrogen bond donors that it has in relation to its alkyl side chain. Because of the low water solubility, the bioavailability and absorption rates are lower than they would be otherwise. The inability of a drug to pass through the cell membrane is a consequence of its low lipophilicity, which is brought on by an excessive amount of hydrogen bond donors (Stewart et al., 2017). In order to swiftly evaluate the possibility for therapeutic use, one might search for conformance with Lipinski's rule, which is often commonly referred to as the rule of 5. This rule determines the number of hydrophilic groups, the molecular weight, and the hydrophobicity of a substance. In accordance with Lipinski's rule of five, the following properties should be present in an active oral medication, as shown in Table 2: The following conditions must be met: (i) the molecular weight must be less than 500 g/mol; (ii) the number of hydrogen bond donors (OH and NH groups) must not exceed five; and (iii) the number of hydrogen bond acceptors (N and O groups) must not exceed five. In addition, the docking scores between the structure of the PfATP4 receptor (the receptor) and all of the compounds that were synthesised (the ligands) are shown in Table 2. When the negative number is larger, it indicates that there is a greater possibility of ligand-receptor interaction. The change in scores that was projected to occur between the amino acids that were included and all of the chemical derivatives that were made it into the PfATP4 pocket was, in fact, seen.

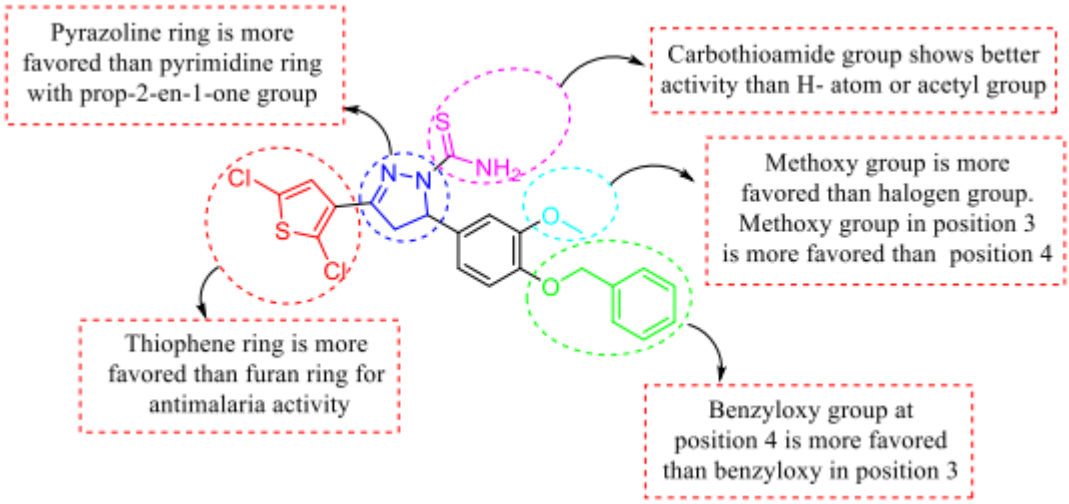


Fig. 2 The results obtained from different structure compounds model.

Table : 1 Compound Resistance Data for IC 3D7 and IC RKL9

Compound	IC 3D7 (µg/mL)	IC RKL9 (µg/mL)	Resistance Index (IC 3D7/IC RKL9)	CQ (Chloroquine Diphosphate)
Chloroquine Diphosphate	20.63	36.11	0.1	20.63
Artemisinin	4.51	8.46	1.0	4.51
Compound 1	84	19	4.2	2.0
Compound 2	5.2	24	4.1	1.2
Compound 3	22.2	24	6.4	3.5
Compound 4	14.1	23	6.5	3.2
Compound 5	6.2	15	2.2	2.8
Compound 6	9	3.4	1.2	1Aiii
Compound 7	2.1	8	1.1	1.9
Compound 8	6.3	14	29	2.1
Compound 9	18	9.9	19.7	6.1
Compound 10	2.1	15	4.3	0.48
Compound 11	4.9	14	36	13
Compound 12	2.4	2.2	2Bi	4.2
Compound 13	4.2	9	2.2	1.7
Compound 14	18.2	16	7.3	24
Compound 15	16.2	15.2	5.5	2.9
Compound 16	7.6	14.4	3.4	2.2
Compound 17	3B	20	10.5	1.9
Compound 18	12.2	34.2	5.4	2.2
Compound 19	3.2	11	29	1.1
Compound 20	4AH	6.2	14	2.9
Compound 21	2.1	4.9	13	2.5
Compound 22	22	1.1	2.0	4Bi
Compound 23	44	10	3.2	13
Compound 24	5.1	12	20	2.5

There was a substantial affinity for the active site of PfATP4 among all of the compounds that were investigated, with free binding energies ranging from -11.05 to -8.56 kcal/mol. The molecules 1Aiii, 1Bi, and 1A were notable since their free binding energies were 9.64, 11.05, and -10.35 kcal/mol, respectively. There have been a few efforts made to construct a series of chalcone, pyrazoline, and pyrimidine derivatives using various scaffolds consisting of thiophene, furan, and methoxyphenyl that are joined at both ends. It can be shown in Figures 3-5 that the aromatic ring in compounds 1, 1Aiii, and 1Bi was responsible for the formation of hydrophobic interactions in the binding site of 2DQS.PDB. Two p-r bonds were formed with ILE 235 and PRO 681 by Chacone, which was the first chemical to be docked. Additionally, three hydrogen bonds were formed with ASN 201, ASN201, and ARG 489 each. It was determined that the thiol groups of chemical 1 and VAL 679 formed a single p-lone pair bond with them other. Compound 1 docked to ARG 678 and VAL 200, where it produced three hydrogen bonds with ASN 201, VAL 679, and GLU 680. Additionally, it created two p-alkyl alkyl bonds from these two substrates. Additionally, a single carbon-hydrogen bond was formed by the combination of Compound 1 with LEU 180. Further, compound 1Aiii was able to dock with ARG 489 and make two p-cation connections. Additionally, it was able to form three hydrogen bonds with ASN 201, VAL 679, and GLU 680. One hydrogen bond was formed between the thiol group of compound 1Aiii (pyrazoline) and the thiol group of ASN 201 resulting in the formation of the compound. Additionally, compound 1Aiii docked with ILE 235, PRO 681, VAL 200, and LEU 180, resulting in the formation of four alkyls and p-alkyl linkages in total. This was in addition to the formation of one van der Waals bond with GLU 680. According to the docking data, compound 1Bi (pyrimidine) formed two hydrogen bonds with ASP 703 and ASP 707, two p-cation and p-anion links with LYS 684, and two with ASP 351. Additionally, the compound formed two bonds with ASP 351. Through the formation of a single sulfur-X bond, the thiol group of compound 1Bi was connected to the thiol group of THR 353. One of these links was seen during docking. Compounded 1Bi generated a carbon-hydrogen connection with VAL 679, one van der Waals bond with GLU 680, and three alkyl-p-alkyl bonds with VAL 200, LYS 352, and PRO 681. Additionally, one of these bonds was observed during that process.

It is important to have strong and stable contacts inside the active site in order to decrease 2DQS activity, and these bondings achieved that level of interaction. During the in vitro experiment, the cytotoxic impact of Compound 1Aiii and ASN 201 was attributed to the hydrogen bond interaction that took place between the two compounds in the active site of PfATP4.

Unless otherwise noted, all solvents and reagents were purchased that were of an analytical quality, and they were used without any further purification.

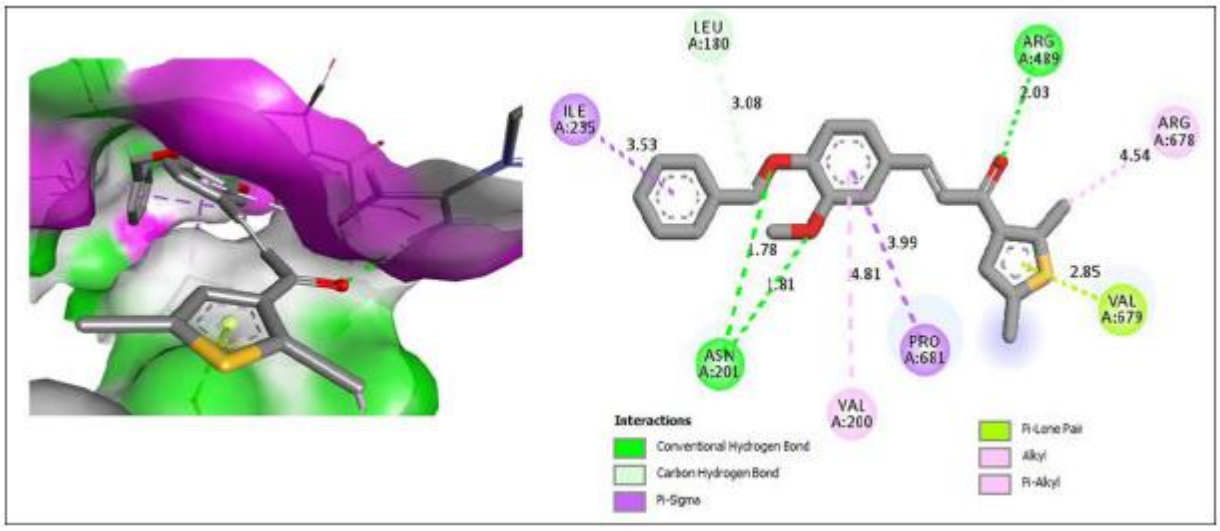


Fig. 3 The best predicted binding poses of (a) 2D- and (b) 3D-molecular structure interaction of compounds 1 with 2DQS.PDB. In the scaffold, green color represents the carbon atoms, red for oxygen, sky blue for fluorine, dark blue for chlorine, and pale blue for the nitrogen atom.

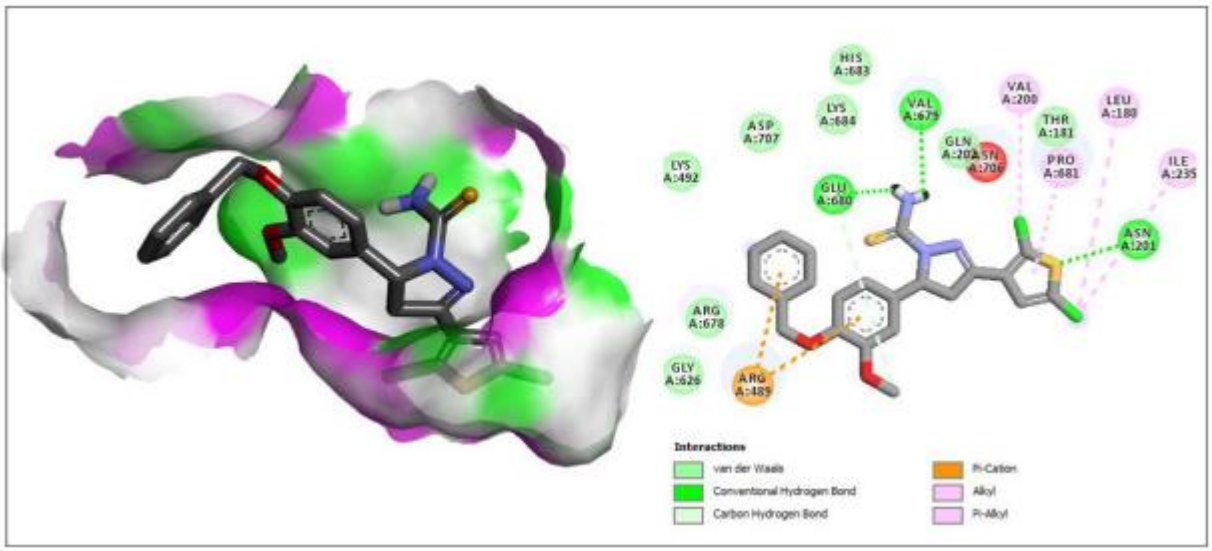


Fig. 4 The best predicted binding poses of (a) 2D- and (b) 3D-molecular structure interaction of compounds 1Aiii with 2DQS.PDB. In the scaffold, green color represents the carbon atoms, red for oxygen, sky blue for fluorine, dark blue for chlorine, and pale blue for the nitrogen atom.

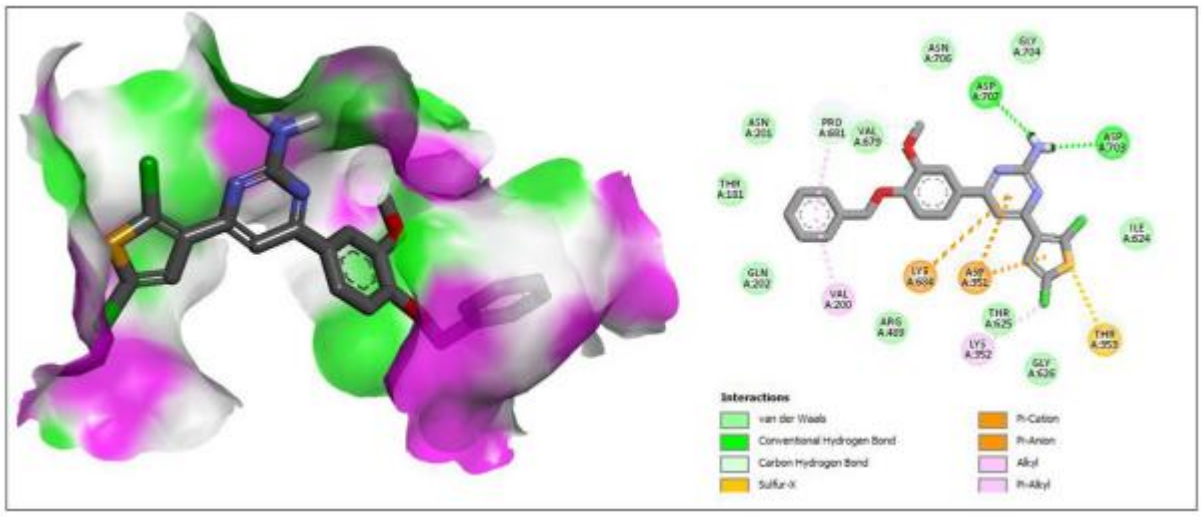


Fig. 5 The best predicted binding poses of (a) 2D- and (b) 3D-molecular structure interaction of compound 1Bi with 2DQS.PDB. In the scaffold, green color represents the carbon atoms, red for oxygen, sky blue for fluorine, dark blue for chlorine, and pale blue for the nitrogen atom.

For the purpose of monitoring the reaction process, Thin Layer Chromatography (TLC) paper, silica gel, and Kieselguhr coated with fluorescent indicator F254 were used. Under the assistance of a UV light equipment, spots were seen. The Melting point (Stuart SMP10) apparatus was used in order to ascertain these melting points, which have not been altered for any reason. When recording the NMR spectra, the Bruker-Advance 500 MHz UltrashieldTM spectrometer was used as the instrument of choice. Tetramethylsilane served as the internal reference system, and the solvents that were used were either DMSO d6 or CDCl3. For the purpose of quoting chemical shifts (d), a reference to TMS is used. The definitive 13C designations were established on the basis of the findings of the research. Through the use of an Attenuated Total Reflection (ATR) Nicolet 6700 Fourier Transform Infrared (FT-IR) spectrometer that operates within the frequency range of 600-4000 cm1, it was feasible to recognise the absorption bands of the functional groups.

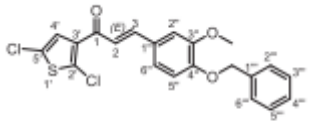
FUNDING AND RESULT

The Claisen-Schmidt condensation (Scheme 1) is used to carry out the reaction. This condensation takes place in 25.0 mL of ethanol with NaOH serving as a catalyst. The reaction is carried out between 0.01 mol of 3-acetyl-2,5- dichlorothiophene or 2-acetylfuran and either 4-benzyloxy-3-methoxybenzaldehyde or 3-benzyloxy-4-methoxybenzal dehyde. At room temperature, the reaction mixture was agitated for a period of time ranging from six to twenty-four hours. Through the use of TLC, we were able to monitor the progression of the reaction. Following the process of filtering, washing with cold water, and drying, the

solid that was produced emerged with a yellow hue. The process of recrystallising the solid product from methanol resulted in the production of a yellow powder.

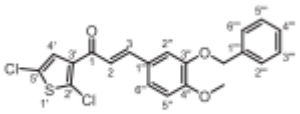
Scheme 1 Synthesis of chalcones 1–4.

3-(4-(benzyloxy)-3-methoxyphenyl)-1-(2,5-dichlorothiophen-3-yl)prop-2-en-1-one, 1.



71% of the total was produced. Bright yellow colour throughout. C.p.: 118–123 degrees Celsius, MW: 419.32. FT-IR (cm1): 3032 (Csp2 -H str.), 2881 (Csp3 -H str.), 1644 (C = O str.), 1510 (C = C str.), 989 (C-O str.), and 694 (C-Cl str.). 1 H NMR (500 MHz, CDCl3) d, ppm: 3.97 (s, CH3, 3H), 5.24 (s, CH2, 2H), 6.92 (d, J = 8.5 Hz, H-3, 1H), 7.16 (t, J = 3.0 Hz, H-20 ", H-60 ", 2H), 7.18 (d, J = 2.0 Hz, H-50 ', 1H), 7.20 (s, H-20 ', 2H), 7.24 (s, H-40 , 1H), 7.35 (d, J = 7.5 Hz, H-60 ', 1H), 7.41 (t, J = 7.0 Hz, H-40 ", 1H), 7.46 (d, J = 7.5 Hz, H-30 ", H-50 ", 2H), 7.70 (d, J = 15.5 Hz, H-2, 1H). 13C NMR (125 MHz, CDCl3) d, ppm: 56.1 (CH3), 70.8 (CH2), 110.8 (C-20 '), 113.4 (C-50 '), 121.8 (C-2), 123.2 (C-60 '), 126.9 (C-30), 127.1 (C-50), 127.2 (C40), 127.7 (C-20 ", 60 "), 128.1 (C-10 '), 128.7 (C-40 "), 130.6 (C30 ", 50 "), 136.4 (C-10 "), 138.0 (C-20), 145.7 (C-3), 149.8 (C40 '), 150.9 (C-30 '), 184.0 (C-1). CHN chemical analysis consists of: This is what the results for C21H16Cl2O3S looked like: 60% of the total is copper, while 3.85% is hydrogen. C: 59.85% and H: 3.55% were discovered.

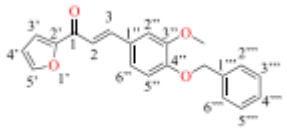
(E)-3-(3-(benzyloxy)-4-methoxyphenyl)-1-(2,5- dichlorothiophen-3-yl)prop-2-en-1-one, 2.



83% is the result. The solid yellow hue of this material is accompanied with a melting point that falls anywhere between 175 and 180 degrees Celsius. Preheat to 419.32 degrees Celsius. There are the following infrared spectra (m, cm-1): 3102 and 3028 (Csp 2-H str.), 2923 and 2833 (Csp 3-H str.), 1643 (C = O str.), 1571 (C = C aromatic atr.), 1506 (C = C alkenyl str.), 1137 (C-O), 1007 (C-S), and 812 (C-Cl.). A 1H NMR spectra was acquired using CDCl3 at a frequency of 500 MHz, as shown below: There were 3.96 parts per million for s-CH3, 2.93 parts per million for d, 7.12–7.49 parts per million for m, 7.65 parts per

million for d, and J = 15.5 Hz for H–3, 1H. 13C NMR (125 MHz, CDCl3) d, ppm: 56.0 (CH3), 71.2 (CH2), 111.5 (C-50 '), 112.9 (C-20 '), 121.5 (C-2), 124.0 (C-60 '), 126.8 (C-30 '), 127.2 (C-50), 127.2 (C-40), 127.3 (C-10 '), 128.1 (C-20 ",60 "), 128.7 (C-40 "), 130.7 (C-30 ",50 "), 136.7 (C-10 "), 138.0 (C-20), 145.5 (C-3), 148.3 (C-40 '), 152.4 (C-30 '), 183.8 (C-1). An analysis of the CHN element for C21H16Cl2O3S revealed the following values: H: 3.85%; C: 59.80%; H: 3.55%; both of these values were found by computation.

(E)-3-(4-benzyloxy)-3-methoxyphenyl)-1-(furan-2-yl) prp-2-en-1-one, 3.



The return was 68.6%. a colour that is 100% yellow. 117–122 degrees Celsius is the melting point. Fourier transform infrared spectroscopy (ATR, cm1): 3022–3155 (C–H sp 2), 2847–2980 (C–H sp 3), 1653 (C = C str.), 1583 and 1509 (C = C str.), 1009 (C–O str.)\ 1. 1 H NMR (500 MHz, CDCl3) d, ppm: 3.94 (s, CH3, 3H), 5.21 (s, CH2, 2H), 6.67 (dd, J = 1.5 Hz, 5.0 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 9 Hz, 1H), 7.26 (dd, J = 3 Hz, J = 7.5 Hz, 1H), 7.29 (d, J = 3.5 Hz, 1H), 7.34 (d, J = 7.5 Hz, 1H), 7.40 (t, J = 15 Hz, 2H), 7.48 (d, J = 7.5 Hz, 2H), 7.65 (s, 1H), 7.77 (s, 1H). Based on the 13C NMR spectra obtained in CDCl3 at 125 MHz, the following chemical shifts are observed: 56.1 (CH3), 71.3 (CH2), 111.6 (C-20'), 112.5 (C-40), 113.3 (C-50'), 117.1 (C-30), and 119.1 (C-2) are the constituents of the carbon series. The following values are obtained from the synthesis, characterisation, and biological evaluation of new chalcone, pyrazoline, and pyrimidine compounds that are shown in Scheme 1. 7 The following values are available: 123.6 (C-60'), 127.5 (C-20", C-60"), 127.7 (C-10), 128.1 (C-40", 128.7 (C-30", C-50"), 136.7 (C-10"), 144.0 (C-3), 146.3 (C-40'), 148.4 (C-50), 152.2 (C-30'), 153.9 (C-20), and 178.1 (C-1). C: 75.43% and CH: 5.43% were found during analytical analysis for the compound C21H18O4 (%). C equals 75.12%, and H equals 5.13%, according to the calculation.

The growth of malaria parasites in culture was measured using the SYBR-Green-I assay, which is based on microtiter plates. This was done in order to evaluate the antimalarial activity of the materials and processes that were used in the creation of anti-malaria drugs.

CONCLUSION

There is a significant amount of significance that the heterocycles that are known as pyrimidines have in the domains of biology and medicine. The therapeutic properties of a large variety of pyrimidine drugs each have their own unique set of features. During the process of evaluating the antibacterial properties of 5-ethoxy carbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidine-2-(1H)-one, a positive outcome was observed.The reaction between 3-acetyl-2,5-diphenylthiophene (1-2) and 2-acetylfuran (3-4) with either 4-benzyloxy-3-methoxybenzaldehyde or 3-ben zyloxy-4-methoxybenzaldehyde, respectively, ultimately led to the formation of a series of four chalcones (1-4). All of these chalcones, 1-4, were put through further cyclocondensation processes with hydrazine hydrate derivatives in order to produce twelve more pyrazoline derivatives, (1-4)A(i-iii). The reaction of these chalcones with guanidine or thiourea resulted in the production of eight new pyrimidine derivatives, which were designated as (1-4)B(i-ii). All of the compounds were investigated by using FT-IR, 1 H, and 13 C nuclear magnetic resonance spectroscopy. Each of the synthetic compounds was examined to see whether or not they have the capacity to eliminate malaria cells. The most active of the pyrazoline compounds (1-4)Aiii) that contain carbothioamide functionality is pyrazoline 1Aiii, which has an IC50 3D7 value of 2.1, an IC80 3D7 value of 8, and an IC50RKL9 value of 1.1. Compared to any of the chalcones 1-4 on their own, heterocyclic compounds that were produced from chalcones 1-4 have shown much higher levels of antimalarial activity against P. falciparum. The activity of compounds that had a methoxy group in the para position was found to be much higher than that of compounds that contained a methoxy group in the meta position. Research conducted using molecular docking indicates that a larger molecule has a greater number of bonds, which indicates that it interacts with a greater number of amino acid residues in the active site of PfATP4. It is possible that this is the reason why a chemical with a bigger structure is more effective against malaria. As an additional point of interest, the docking scores revealed that the binding energies of the three compounds (1Aiii, 1Bi, and 1) to the PfATP4 receptor were the highest among all of the derivatives that were synthesised.

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