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Date – 28th Feb 2026

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Rani Channamma University, Belagavi

Faculty Development Programme

Certificate of Participation

This is to certify that **Dr. Dr. BINDU P J** has participated in the One Week Faculty Development Programme (Online) on "**Roles of Chemical Science Towards Sustainable Development for Viksit Bharat**" organized by the **Department of Chemistry**, under PM-USHA (MERU) – Grant, held during **5th January 2026 to 10th January 2026** at Rani Channamma University, Belagavi.

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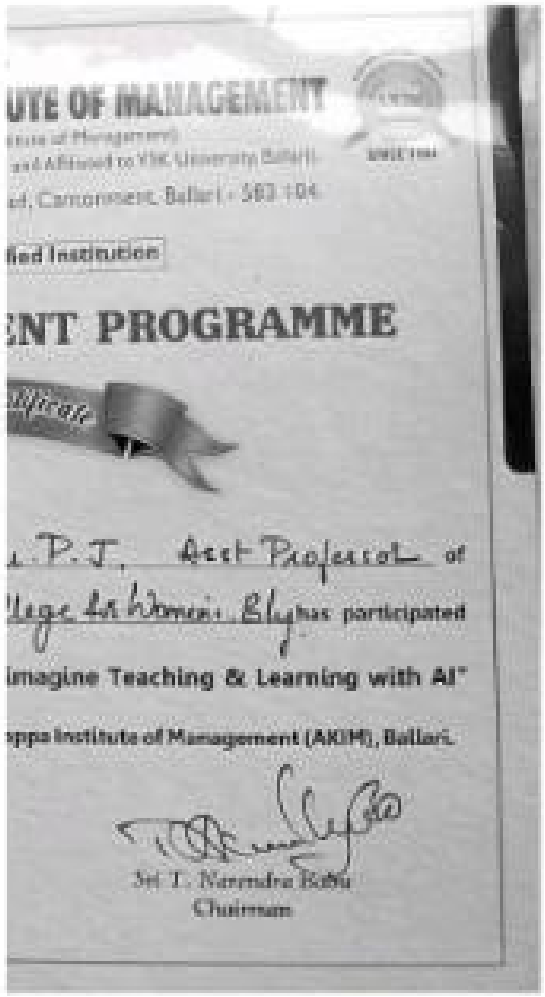
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Affiliated to ~~Karnataka State Akkamahadevi Women~~ *University Participated in the Online Interdisciplinary Refresher Course in Biological Sciences from 17-03-2025 to 29-03-2025 (12 working days) organized by UGC-Malaviya Mission Teacher Training Centre, Karnatak University, Dharwad and Obtained Grade* 'A'.

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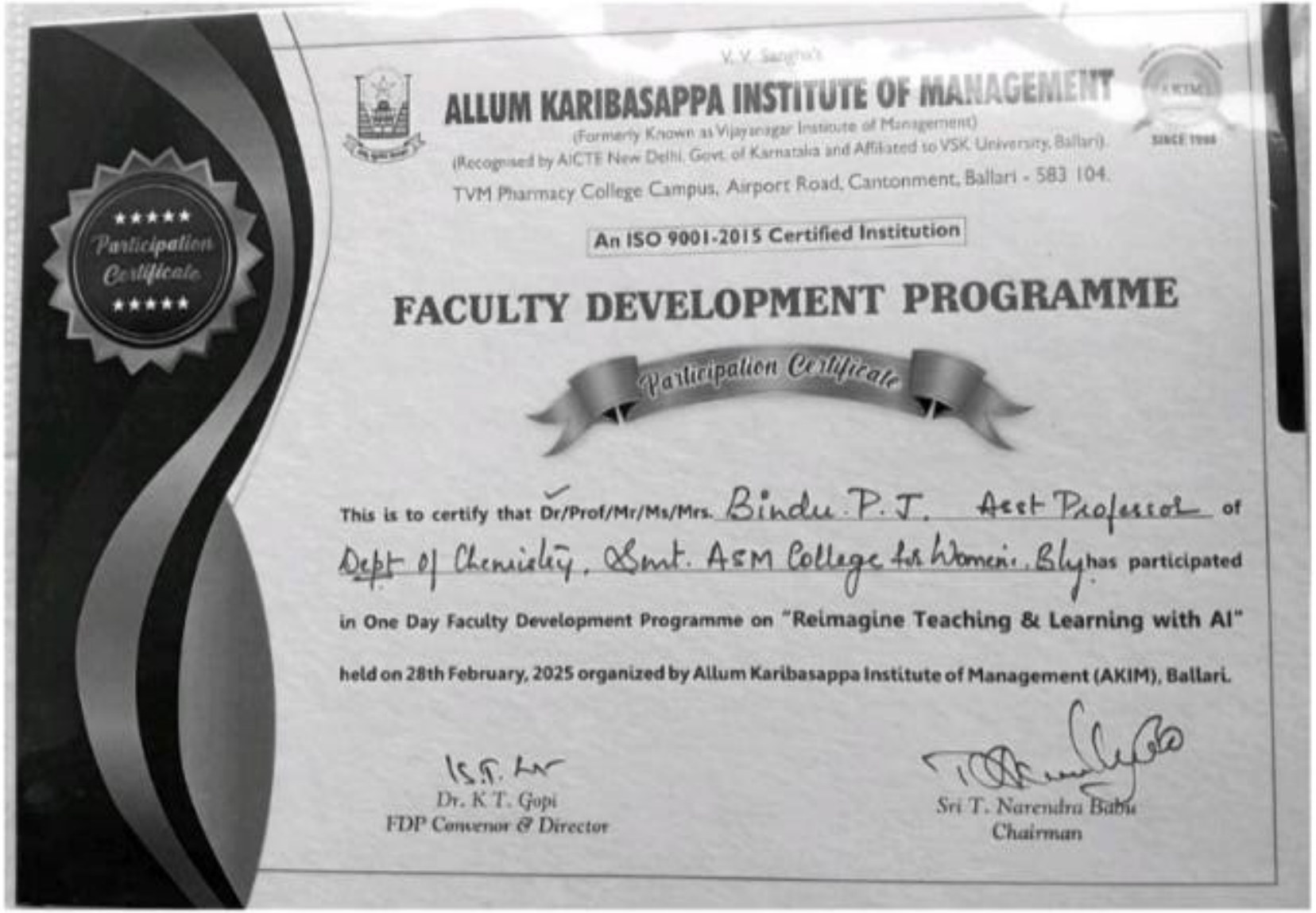
This is to certify that Prof. / Dr/Mr/Mrs. Dr. Bindu P.J. Asst. Professor.
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has participated / Orgnized the State level Five days online Faculty Development Program on
"Research Methodology" (PM USHA Funded Program) held from 03-03-2025 to 07-03-2025

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FDP & IQAC
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Chemistry " held on 29 & 30th April, 2025 organized by Department of Chemistry, Veerashaiva College,

Ballari.

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Convener & HOD Department of Chemistry
Veerashaiva College, Ballari.

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KARNATAK UNIVERSITY DHARWAD

Department of Botany

CERTIFICATE

OF PARTICIPATION

THIS CERTIFICATE IS PROUDLY PRESENTED TO:

Dr. BINDU P. J.

Akkamahadevi Womens University, Vijayapura

for actively participating in the "One Day National Seminar on Current Trends in Algal Research " on 10th January 2025 held at the Department of Botany, Karnatak University, Dharwad, Karnataka.

Dr. Sreenivasa Nayaka
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(Oral / Poster) Paper On Topic Design, Synthesis & molecular docking studies of 2,5-Diarylthiazole In One Day
National Level Conference On "Frontier's In Agriculture, Medical & Environmental Sciences (FAMES-2k25)" organized by
IQAC in association with Departments of Botany and Zoology on 28th November 2025.

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CERTIFICATE OF APPRECIATION

International Conference on Sustainable Energy and Environmental Technologies 2025 (ICSEET-2025)
(8th REVA Research Conclave)

This is to certify that Dr. BINDU. P. J, Asst. Professor, of Smt. A.S.M. college, Ballari has participated/presented oral/poster in the International Conference on **Sustainable Energy and Environmental Technologies 2025 (ICSEET-2025)** held at REVA University from of December 11 - 13, 2025

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Biomedical and
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Antimicrobial, antioxidant and molecular docking studies of Karanjin derivatives synthesized via Microwave assisted synthesis

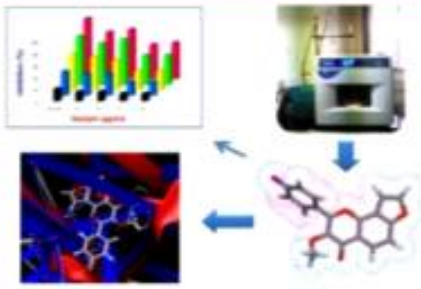
T.R. Ravikumar Naik,*[1] P.J. Bindu,[2]

[1]Department of P. G. Studies in Chemistry, Veerashaiva College, Ballari, VSK University-583 104, India. [2]Department of Chemistry, A.S.M. Women's College, Ballari, Women's University-583 104, India.

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ABSTRACT

Efficient and facile microwave-assisted synthesis of karanjin derivatives were synthesized successfully. The reaction time for synthesis of analogs was drastically reduced from a reported 8–12 hrs to only 30 min. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR and mass spectroscopic analysis. The synthesized karanjin derivatives were evaluated for their antimicrobial, antioxidant and molecular docking studies. The compounds 7a and 7d displayed maximum antimicrobial activities compare to the plant extracted karanjin. In terms of SAR, the presence of a halide group in conjunction with a phenolic group was seen as a significant contributor towards increasing the antimicrobial activity. All the compounds (7a-d) were screened for antioxidant activity by DPPH and hydrogen peroxide radical scavenging methods. The karanjin derivatives (7a-d) exhibited prominent IC_{50} value than standard drug ascorbic acid. Furthermore, that developed compounds showed promising antioxidant activity hence could be evaluated for their molecular docking studies.



Keywords: Microwave irradiation, Karanjin, Pongamia pinnata, Antimicrobial, Antioxidant, Molecular docking.

INTRODUCTION

Natural products have been used to treat human diseases for thousands of years. The results of these treatments have been variable and inconsistent, but advances in pharmaceutical science have seen natural products used as models for the development of new drugs. Even today, in the century of combinatorial chemistry, secondary metabolites of plants, fungi, marine organisms, and microorganisms are still an important source for the development of new drugs.[1-3] About 50 per cent of the drugs introduced to the market during the last 20 years are derived directly or indirectly from small molecules of natural origin.[4]

In the course of our search for bioactive substances from medicinal plant, Pongamia found with diverse applications in medicinal chemistry. *Pongamia pinnata* (L.) [Syn. *Pongamia glabra* (Vent); *Derris indica* (Lamk.)] belongs to family Leguminosae and sub-family Papilionaceae.[5] It is one of the widely grown forest trees with 0.11 million tons of seeds collected every year in India, by states like Andhra Pradesh, Karnataka and Tamil Nadu.[6] Historically, this plant has long been used in India and neighboring regions as a source of Ayurvedic and Sidda medicine.[7] It has a number of medicinal properties and can be used for inhibiting growth of herpes,[8] hypoglycemic, anti-oxidative, anti-ulcerogenic, anti-inflammatory and also shows analgesic properties.[9] Thus, they have gained great importance as clinical therapeutic agents.

Recently, anti-inflammatory effect of karanjin in rat models as substantiated by the inhibition of lipoxygenase-1 and 5-LOX by karanjin,[10] has been reported. Modern pharmacological research proves that, the extract of Pongamia leaves, root, bark, flowers and seeds having furano-flavonoids shows potent pesticidal[11] and insecticidal activity.[12] The biologically active furano-flavonoids like Karanjin, Pongaglabrone and Pongal drug molecules are shown in fig-1.[12]

The microwave-assisted organic synthesis (MAOS) has become an interesting field of the synthetic organic chemistry in recent years, since it allows dramatically reducing the reaction times and increases the yield percentages, compared with conventional synthetic methods.[13]

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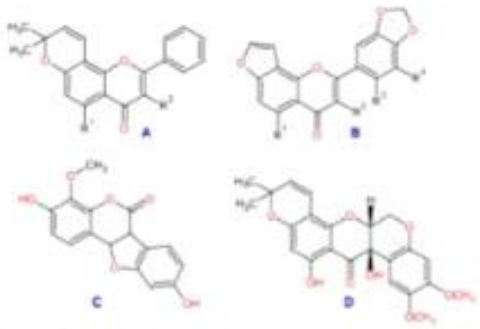


Figure 1. Biologically active furano-flavonoids

The structural modifications of medicinal (natural) compounds by various chemical methods will result in the synthesis of several new drug component derivatives. The chemical synthetic drug compounds have shown to exhibit better pharmacological activities than natural compounds.[14] It is evident from these studies that, the pharmacological properties of karanjin can be expected beneficial.

Recently, we exploited the potential application of karanjins for the synthesis of silver MNPs in medicinal chemistry.[15] Karanja seed oil was used in Ayurvedic and Siddha medicine for its health benefits.[15] Karanjin is the major furano-flavonoid present in the seed oil. Since karanjin is a lipid-soluble component, it was extracted into the karanja oil using petroleum ether.[15]

Nowadays, molecular docking has been applied as a mechanistic tool to study the inhibition of enzymes that negatively affect antioxidant activity, like NADPH oxidase (NO), which is responsible for ROS generation.[16] One of the computational chemistry approaches, known as molecular docking, have recently gained great popularity in the field of modern drug development.[17] These approaches offer many benefits, notably enabling the analysis and interpretation of bioassay data, as well as effectively identifying potential drug targets and discovering new candidate drugs with enhanced therapeutic characteristics.[17] Molecular docking serves as one of the bioinformatics techniques that have been applied widely to explore the interactions between bioactive compounds and the active sites of specific proteins, with the aim of discovering the essential structural features that affect their binding efficiency.[17]

In the present investigation, we report herein the microwave assisted synthesis of karanjin derivatives for efficient biological activities. Taking inspiration from the above and as a part of our continuing research on the synthesis of biologically active compounds.[18-22] Hence, the need to be replaced by newer drugs periodically. From this perspective, we describe the microwave assisted synthesis of pharmacologically important karanjin derivatives (Scheme 1) and studied their antimicrobial, antioxidant and molecular docking studies.

Materials and Methods

Materials and equipment

All the chemicals used in the present study are of AR grade. M/s Sigma-Aldrich, and Merck, USA and M/s S.D. Fine Chem. Pvt. Ltd, Mumbai, India. Calf thymus DNA (CT DNA) and supercoiled pUC19 DNA (cesium chloride purified) were obtained from Bangalore Genei (India). Agarose (low melt, 65°C, molecular biology grade for DNA gels), ethidium bromide, bromophenol blue, Tris(hydroxymethyl)aminomethane (Tris), sodium chloride, ethylene diamine tetraacetic acid disodium salt (EDTA-Na2), sodium azide, were of molecular biology grade, obtained from Himedia (India).

Melting points were recorded on an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analyses were carried out using a Perkin-Elmer 240C CHN analyzer. IR spectra were recorded on a FT-IR infrared spectrophotometer. ^{1}H-NMR spectra were obtained using 300 MHz and 400 MHz on a Bruker spectrometer (chemical shifts in δ ppm). Mass spectra were recorded using a micro spray Q-TOF MS ES Mass spectrometer.

Experimental

General procedure for the synthesis of 1-[4-(2,2-diethoxyethoxy)–2–hydroxyl phenyl] ethanone (2a):

Resacetophenone (**1a**) (2 g, 0.329 mol) was taken in dry DMF (15 ml) at 0°C followed by the addition of anhydrous K_2CO_3 (5 g, 0.49 mol) and stirred for 20 min. After 20 min, bromoacetaldehyde diethyl acetal (3.1 g, 0.39mol) was added drop wise at 0°C. After completion of addition, the reaction mixture was allowed to come to room temperature and finally the reaction mixture was transfer in 50 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 30 minutes. The progress of the reaction was monitored by TLC. After completion of reaction (30 min), the reaction mixture was filtered. The filtrate was solubilised in chloroform and washed with brine solution. The chloroform layer was dried over anhydrous sodium sulphate, evaporated using rotary evaporator and purified by silica gel column chromatography using petroleum ether:ethyl acetate (10:3) as eluent. The desired product **2a** is obtained as white solid in 80 % yield. ^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.60 (1H, s, chelated OH), 7.59 (1H, d, J = 9.06 Hz), 6.36–6.44 (2H, m), 4.78 (1H, t, H-2), 3.98 (2H, d, J = 5.29 Hz, H-1), 3.56–3.75 (4H, m, –O–CH_2–CH_3), 2.53 (3H, s, –CO–CH_3), 1.23 (6H, t, –O–CH_2–CH_3).

Synthesis of 1-(4-hydroxy-1-benzofuran-5-yl)ethanone and **1-(6-hydroxy-1-benzofuran-5-yl)ethanone (3a and 4a)**:

1-[4-(2,2-Diethoxy-ethoxy)-2-hydroxy-phenyl]-ethanone (**2a**) (1g, 1 eqt) was irradiated for 30 minutes in dry toluene (15 ml) with Amberlyst 15 (125 mg) with concurrent removal of water using Dean-Stark trap for 30 minutes. The resulting reaction mixer was filtered and the resin was washed with excess of toluene. The filtrate thus obtained was concentrated to dryness and two pure compounds were isolated by silica gel column chromatography using ethyl alcohol-petroleum ether (1:10) as eluent. The desired products **3a** and **4a** is obtained as yellow solid in 70:30 % yield. The ^{1}H NMR of **4a** is as follows; (400 MHz,

DMSO-d_6): δ = 2.16 (s, 3H, CH_3), 7(d, 1H, H-3), 7.04 (d, 1H), 7.26(s, H), 7.56 (d, 1H), 7.64 (d, 1H), 13.28 (s, 1H, OH).

Synthesis of (2E)-1-(4-hydroxy-1-benzofuran-5-yl)-3-phenylprop-2-en-1-one (5a):

To a solution of 1-(4-hydroxy-1-benzofuran-5-yl)ethanone (**3a**) (1.0 g, 1 eqt) and benzaldehyde (0.149 g, 1 mmol) were dissolved in absolute ethanol (7 mL) in a microwave reaction vessel (10 mL) fitted with a suitable magnetic stir bar, followed by the addition of KOH (50%, 5 mmol). The microwave reaction vessel was capped properly and placed in the proper position in the microwave oven, and the pressure sensor was placed over the microwave vial. The yellow precipitates were collected in a suction filtration and washed with cold ethanol/water 1:1 (3×5 mL). The resulting precipitates were air-dried to yield 80% of desired compounds, mp 170–172 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.75 (d, J = 9.0 Hz, 2H, 3'-H, 5'-H), 6.95 (m, 1H, 5-H), 6.97 (d, J = 7.0 Hz, 1H, 3-H), 7.52 (m, 1H, 4-H), 7.73 (d, J = 9.5 Hz, 2H, 2'-H, 6'-H), 7.74 (d, J = 14.5 Hz, 1H, CH = CH-C = O), 7.81 (d, J = 15 Hz, 1H, CH=CH-C = O), 8.24 (d, J = 8.0 Hz, 1H, 6-H), 13.09 (s, 1H-OH). ^{13}C NMR (DMSO-d_6) δ = 39.8, 111.9, 114.8, 122.0, 117.8, 119.0, 120.6, 121.8, 130.5, 131.5, 135.9, 147.0, 152.5, 162.4, and 193.3.

Synthesis of 3-hydroxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (6a-d):

To a solution of **5a** (1.0 g, 1 eqt) in ethanol (15 ml) was added hydrogen peroxide (30%, 0.25 eqts, i.e., 0.5g) in the presence of potassium hydroxide (1 M, 0.5 eqt) at 0°C and stirred for 10 min. After completion of addition, the reaction mixture was allowed to come to room temperature and finally the reaction mixture was transfer in 50 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 20 minutes. The progress of the reaction was monitored by TLC. After completion of the reaction quenched with 2N HCl, it was extracted with ethyl acetate (50 ml), dried, and concentrated. The product obtained was purified using column chromatography. The fractions eluted at 30% ethyl acetate in petroleum ether contained pure 3-hydroxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (**6a**).

The specytral data of 3-hydroxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (6a): yellow solid; Yield (75%); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.13 (d, J = 8.8 Hz, 1H), 7.93 (s, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.76 (br s, 1H), 7.60–7.29 (m, 12H, aromatic), 7.08 (br s, 1H), 5.28 (s, 2H, OCH2-Ph), 5.30 (s, 2H, OCH_2-Ph); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 173.0, 158.0, 150.4, 149.9, 148.5, 145.5, 144.0, 137.8, 137.0, 136.7, 128.6 (2C), 128.5 127.3, 127.1, 124.1, 121.4, 116.9, 115.9, 114.2, 114.0, 110.0, 104.1, 71.4.

Synthesis of 3-methoxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (7a):

A mixture of 3-hydroxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (**6a**) (1.4 g, 1 eqt), dimethyl sulphate (0.228 g) and anhydrous potassium carbonate (10 g) in acetone (50 ml) was stirred for 10 min. After completion of addition, the reaction mixture was transfer in 100 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 30 minutes. The completion of the reaction was confiremed by TLC. Solvent acetone was removed by rotary evaporator under under reduced pressure. Approximate 30 ml of water was added to the residue and was extracted with ether. The ether layer was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness. The product obtained was purified using column chromatography using methanol-chloroform (10:1) as developing solvent. It was crystallized from methanol to give yellow crystals.

The specytral data of 3-methoxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (7a): ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.95 (s, 3H, -OCH_3), 6.75 (d, 1H, J = 9Hz, H-6) 7.15 (m, H-4), 7.85 (d,1H, J = 2Hz, H-5), 7.95 (d, 2H, J= 9Hz, H-5); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 173.0, 158.0, 150.4, 149.9, 148.5, 145.5, 144.0, 132.1, 130.0, 128.3, 121.8, 121.2, 119.8, 117.9, 110.0, 104.1, 56.23; MS m/z [M+Na]$^+$ for $C_{18}H_{12}O_5$ calculated: 292.2854 found: 315.2014.

Synthesis of 3-methoxy-2-(4-methylphenyl)-4H-furo[2,3-h]chromen-4-one (7b): ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.20 (1H, d, J = 9 Hz), 8.10 (1H, dd, J =9 Hz, J2=2 Hz), 7.55 (m, 4H), 7.15 (1H, d, J =2 Hz), 3.93 (3H, s), 2.34 (3H, s); ^{13}C NMR (DMSO-d_6 75 Hz): δ = 175.0, 158.1, 154.8, 149.9, 145.7, 141.8, 131.0, 130.6, 128.6, 121.9, 119.7, 117.1, 109.9, 104.2, 60.2, 23.56; MS m/z [M+Na]$^+$ for $C_{19}H_{14}O_5$ calculated: 306.3120 found: 329.2558.

Synthesis of 2-(4-chlorophenyl)-3-methoxy-4H-furo[2,3-h]chromen-4-one (7c): ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.24 (1H, d, J = 9 Hz), 8.16 (2H, dd, J =9 Hz, J2=2 Hz), 7.58 (m, 4H), 7.21 (1H, d J =2 Hz), 3.95 (3H, s); ^{13}C NMR (DMSO-d_6 75 Hz): δ = 175.3, 158.6, 153.5, 150.1, 145.1, 140.5, 130.8, 130.1, 129.3, 121.0, 119.2, 118.0, 110.1, 105.1, 58.41; MS m/z [M+Na]$^+$ for $C_{18}H_{11}ClO_5$ calculated: 326.7305 found: 349.7295.

Synthesis of 2-(4-fluorophenyl)-3-methoxy-4H-furo[2,3-h]chromen-4-one (7d): ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.20 (1H, d, J = 9 Hz), 8.15 (2H, dd, J =9 Hz, J2=2 Hz), 7.58 (m, 4H), 7.16 (1H, d J =2 Hz), 3.94 (3H, s); ^{13}C NMR (DMSO-d_6 75 Hz): δ = 174.9, 159.0, 154.8, 149.9, 145.2, 142.1, 130.8, 130.0, 129.1, 122.1, 120.2, 118.0, 110.1, 104.5, 60.2; MS m/z [M+Na]$^+$ for $C_{18}H_{11}FO_5$ calculated: 310.2759 found: 333.2688.

ANTIOXIDANT ACTIVITY

DPPH Radical Scavenging Activity

DPPH, a stable free radical at room temperature, which produces a purple colour solution in methanol. It is reduced in the presence of synthesized antioxidant molecule, giving rise to uncoloured methanol solutions. In this screening method, activity is measured spectrophotometrically. DPPH has a strong absorption at 517 nm and upon reduction by a free radical scavenging antioxidant, this absorption is decreased. The degree of discoloration indicates the scavenging potential of the antioxidant compounds in terms of hydrogen donating ability.[23] The activity is expressed as percentage of inhibition.[23]

The antioxidant activity of karanjin derivatives on DPPH radical scavenging activity was measured according to the literature method.[23] About 10 mg of compound in 10 ml methanol at different concentrations were prepared. A methanolic solution of DPPH (0.15%) was mixed with different concentrations of

compounds (10, 20,40, 60, 80, 100 µg/mL). The mixture was shaken vigorously and left to stand for 15 min. Absorbance of the resulting solution was measured at 517 nm in a UV–visible spectrophotometer. All measurements were made in duplicates with Ascorbic acid as a positive control. Percentage of inhibition and IC_{50} values of synthesized compounds measured by DPPH free radical scavenging activity method are shown in Table 3.

Hydrogen Peroxide Method

The hydrogen peroxide scavenging ability of different concentrations of compounds were investigated based on the scavenging of the hydrogen peroxide by literature method.[23] A measurement of 80 µL of each concentration of compounds and 20 µL of 10 mM hydrogen peroxide was mixed with 100 µL of phosphate buffer (pH 5.0, 0.1 M) in a 96-microwell plate and the samples were incubated for 5 min at 37 °C. Subsequently, 30 µL of freshly prepared 1.25 mM ABTS and 30 µL of peroxidase were added and incubated for another 10 min at 37 °C. Absorbance of the resulting solution was measured at 405 nm in a UV–visible spectrophotometer. Percentage of inhibition and IC50 values of synthesized compounds measured by Hydrogen peroxide method are shown in Table 3.

Molecular Docking Protocol

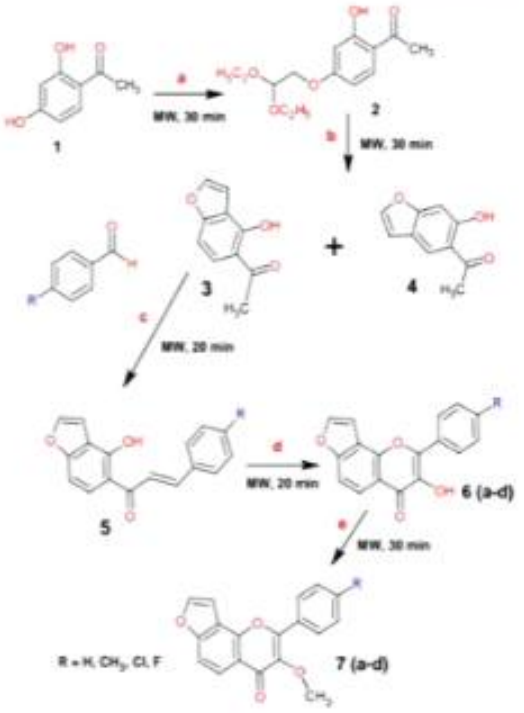
In present study, Autodock was used.[17] Autodock uses an empirical scoring function to calculate binding energy of protein-drug molecule.[17] The crystal structure of NADPH oxidase (PDB ID: 2CDU) was downloaded from Protein Data Bank.[24] Initially, the macromolecule was prepared by removing water molecules and hetero atoms, polar hydrogens were added. In-house synthesized drug molecules were drawn in MDL file (.mol) format using Chemsketch. After docking, conformations were ranked according to their binding energy, and the confirmation with the lowest binding energy was considered as the best docking score. The docking results were visualized using Pymol Visualizer.[17]

Results and Discussion

In our attempts to search for novel antitumor agents, we extended the interest to biological active heterocylces and synthesized series Karanjin derivatives (3-methoxy-2-phenyl-4H-furo[2,3-h]chromen-4-ones) with the aim of evaluating their diverse biological activity.

Chemistry

In recent years, with the development of molecular biology and molecular pharmacology, identifying active pharmaceutical ingredients from medicinal plants has become an important topic of interest in research. In order to further promote the application of karanjin, and find out the mechanism of anti microbial, Pongamia pinnata seeds were extracted, purified, and evaluated for anti-microbial activity. In the current study, we explore the microwave assisted synthesis of 5-acetyl-4hydroxy-benzofuran for the synthesis of biologically active karaanjin. The chemical structures of the isolated and synthesized compounds were confirmed by extensive IR, ^{1}H NMR, ^{13}C NMR and mass spectra. The microwave assisted synthetic path way of the karanjin derivates was shown in scheme 1 (Table 1).



Scheme 1. Reagents and condition: (a) $BrCH_2CH(OEt)_2$, K_2CO_3, DMF, MW, 30 min; (b) Toluene, Amberlyst-15, MW, 45 min; (c) KOH (50 %), Ethanol, MW, 20 min; (d) 30 % H_2O_2, KOH, 0°C, MW, 20 min; (e) Dimethyl sulphate, K_2CO_3, acetone, MW, 30 min.

Table 1. Scope of karanjin and its derivatives

Products[a]	R	Time (min)	Yield(%)[b]	M.P. (°C)
7a	H	30	80	153-155
7b	4-CH_3	30	80	158-160
7c	4-Cl	30	85	152-154
7d	4-F	30	80	149-151

[a]All the products were characterized by elemental analysis, ^{1}H NMR, ^{13}C NMR and Mass spectral studies. [b]Yields of isolated products.

The methanol extract of the dried seeds of Pongamia pinnata was subjected to repeated column chromatography on silica gel, preparative TLC to afford five different compounds. The obtained compound (pale yellow oil) was characterized by different spectroscopic techniques. The IR absorptions at 3444, 1665 and 1635 cm^{-1} indicates the presence of carbonyl groups, respectively. The ^{1}H and ^{13}C NMR spectra showed the presence of methoxy functionl group at δ_H 3.8 (d, J = 8.5 Hz, 3H) and aromatic protons at δ_H 7.26, 6.53, 6.36, 6.31, 6.08 and 5.59. The ^{13}C NMR spectrum (see the Supporting information) exhibited one methoxy (δ_C 56.00 and aromatic at (δ_C 128.3 and 125.7).

Further, we explore, fast and greener microwave assisted approach for the synthesis of an intermediate compound 5-acetyl-4hydroxy-benzofuran for karanjin synthesis (Scheme 1). In literature, the conventional synthesis of 5-acetyl-4hydroxy-benzofuran reported with longer time duration and side product.

In order to overcome the above shortcomings, microwave method was introduced in present study for the synthesis of 5-acetyl-4hydroxy-benzofuran to produce karanjin. Due to the remarkable selectivity and specificity, microwave assisted synthesis has been frequently used in the organic chemistry for several decades,[25] and has been demonstrated to be an effective and practical tool in the development of green chemistry.[26] However, there has been no report on the microwave assisted synthesis of 5-acetyl-4hydroxy-benzofuran of karanjin.

The microwave assisted synthesis of 5-acetyl-4hydroxy-benzofuran could be a promising protocol for the efficient synthesis of karanjin, a potential antimicrobial candidate with considerably improved activity than natural extract. An overall reaction procedure was outlined in Scheme 1. In the present study, karanjin derivatives were prepared by chemical methods and tested for their antimicrobial, antioxidant and molecular docking studies. The attempts to modify karanjin under microwave conditions, the reaction in the presence of BrCH$_2$CH(OEt)$_2$ reacted with potassium carbonate in DMF results compound 2a. Further, we followed 1-[4-(2,2-Diethoxy-ethoxy)-2-hydroxy-phenyl]-ethanone (2a) was irradiated for 30 minutes in dry toluene with Amberlyst with concurrent removal of water using Dean-Stark trap for 30 minutes. The obtained compound (3a) and substituted benzaldehydes were dissolved in absolute ethanol and irradiated in a microwave to results chalcones. Further, we treated compound 5a with hydrogen peroxide in the presence of potassium hydroxide. After completion of addition, the reaction mixture was allowed to come to room temperature and finally the reaction mixture was transfer in 50 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 20 minutes. Finally the 3-hydroxy-2-phenyl-4H-furo[2,3-h]chromen-4-one (6a) and dimethyl sulphate with anhydrous potassium carbonate in acetone was placed in CEM mars microwave and reaction mixture was irradiated for 30 minutes to result title compounds.

Structure Activity Relationship (SAR) with karanjin and chemically synthesized molecules of karanjin showed that the presence of halide group play a major role in antimicrobial activity. SAR also indicates that the structural characteristics, such as the degree of saturation, the side chain length of **7a** and **7d** and the geometric isomerism, appear to play a role in determining the toxicity of **7a** and **7d** karanjin molecules to micro organisms.

Table 2. Antimicrobial activity of karanjin and its derivatives

Compound*	Zone of inhibition (mm) µg ml					
	Bacteria			Fungi		
	1	2	3	4	5	6
Plant extracted karanjin	18	20	17	16	21	18
7a	21	24	19	22	23	19
7b	13	20	14	18	18	15
7c	10	15	11	15	14	10
7d	16	19	19	20	17	17
Amoxycilin	26	23	24	—	—	—
Flumequine	—	—	—	19	23	20

1 - Pseudomonas aeruginosa 2 - P. stutzeri 3 - Escherichia coli 4 - Aspergillus flavus 5 - A. niger 6 - Fusarium solani

The plant extracted karanjin and chemically synthesized Karanjin compounds (scheme 1) were evaluated against a set of common pathogenic microorganisms, including three bacteria: *Pseudomonas aeruginosa*, *P. stutzeri*, *Escherichia coli* and three fungi: *Aspergillus flavus*, *A. niger* and *Fusarium solani* adopting standard protocols[24] along with Amoxycillin (30 µg/disc) and flumequine (30 µg/disc) as positive references for bacteria and fungi, respectively. The pure bacterial and fungal strains were maintained on Nutrient agar and sabouraud dextrose agar (SDA), respectively.

Table 3. Antimicrobial activity of karanjin derivatives and Binding affinities of NADPH oxidase (PDB ID: 2CDU).

Compound*	DPPH Method % of inhibition	IC$_{50}$ value	H_2O_2 Method % of inhibition	IC$_{50}$ value	Binding Energy (Kcal/mol)
Plant extracted karanjin	61.74	2.38 ± 0.02	48.36	2.41 ± 0.04	−7.9
7a	68.15	2.58 ± 0.04	52.14	2.65 ± 0.10	−8.6
7b	72.09	2.68 ± 0.02	56.17	2.84 ± 0.18	−8.9
7c	54.61	3.28 ± 0.12	39.10	4.20 ± 0.10	−10.2
7d	49.22	3.88 ± 0.04	38.89	4.20 ± 0.04	−10.4
Ascorbic acid	80.64	1.52 ± 0.14	76.60	1.44 ± 0.40	−7.0

The antibacterial and antifungal activity was performed, and minimum inhibitory concentration (MIC) was determined (Table 2). The compound **7a** showed a good activity against bacteria and fungi followed by **7d** as compared to the plant extracted karanjin.

In-vitro antioxidant activity of karanjin derivatives.

As explained in the introduction section, free radicals have showed significant interest among scientists in the past decade. Their broad range of effects in biological system has drawn the attention of many experimental works. It has been proved that these mechanisms may be important in the pathogenesis of certain diseases and ageing. There are many reports that support the use of antioxidant supplementation in reducing the level of oxidative stress and in slowing or preventing the development of complications associated with diseases.

DPPH radical scavenging activity

DPPH, a stable free radical at room temperature, which produces a purple colour solution in methanol. It is reduced in the presence of synthesized antioxidant molecule, giving rise to uncoloured methanol solutions. The DPPH has a strong absorption at 517 nm and upon reduction by a free radical scavenging antioxidant, this absorption is decreased. We found that, they exhibited free radical scavenging activity against the stable free radical DPPH. Figure 2 and Table 3, summarizes the 50% inhibition (IC$_{50}$) value of **7a** IC$_{50}$ 2.58 ± 0.04 µg /mL, **7b** IC$_{50}$ 2.68 ± 0.02 µg /mL, **7c** IC$_{50}$ 3.28 ± 0.12 µg /mL and **7d** IC$_{50}$ 3.88 ± 0.04 µg /mL. In the present study results on DPPH free radical scavenging activity shows that the compound **7a** and **7b** are greater scavenging activity than Ascorbic acid.[25,26]

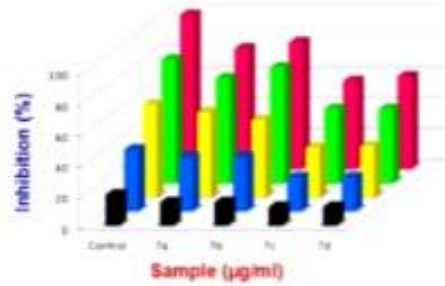


Figure 2. DPPH radical scavenging activity of Karanjin derivatives (7a-d).

Hydrogen peroxide (H_2O_2) scavenging activity

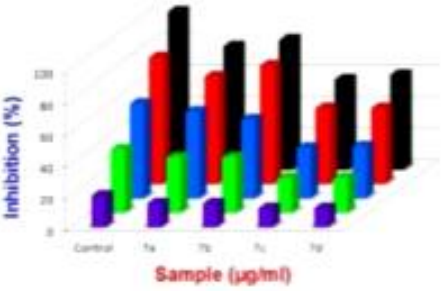


Figure 3. Hydrogen peroxide radical scavenging activity of Karanjin derivatives (7a-d).

H_2O_2 is freely diffusible across membranes and thus may cause oxidative stress in neighboring cells. Quenching of H_2O_2 increases as the concentration increases with the decrease of absorbance at 420 nm. The percent mole ratio of compound **7a** and **7b** are higher than Ascorbic acid. H_2O_2 scavenging activities of **7a** (IC_{50} 2.65 ± 0.10 mg/mL) and **7b** (IC_{50} 2.84 ± 0.18 mg /mL) were significantly ($p<0.05$) higher than Ascorbic acid (IC_{50} 1.44 ± 0.40 mg/mL) as shown in Figure 3 and Table 3.[26]

SAR studies showed karanjin derivatives nuclei at the position of 4 phenyl groups with specific hydrophilic groups increased activity compared to other hydrophobic groups. The DPPH radical scavenging activity of karanjin and its derivatives were found to be linear and dose-dependent. Karanjin showed lower scavenging activity compared to its derivatives. Antioxidant activity is expressed as percentage of inhibition. Compounds (**7a, 7b, 7c** and **7d** in Figure 2 and Figure 3) exerted enhanced activity in comparison to standard drug. Structural activity relations observation demonstrates antioxidant activity depends on electronic factor of substituent aromatic benzene ring. Incorporation of electron releasing substituent at para position improved activity compared to unsubstituted analogue. Introduction of electron withdrawing substituent at para position lowers activity. Antioxidant activity of synthesised compounds and IC_{50} values of synthesised compounds are presented in Table 3. Target compound showed excellent antioxidant activity.

Compound (**7a** and **7b**) recorded lowest IC_{50} value than standard drug Ascorbic acid and could be an efficient antioxidant.[26]

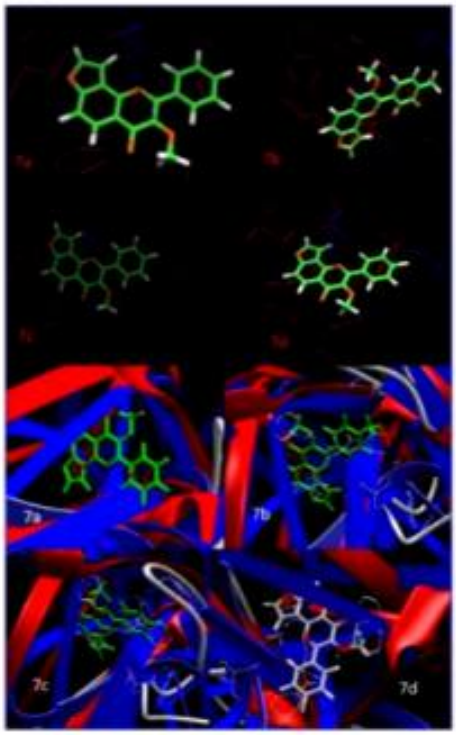


Figure 4. Molecular Docking Interaction diagram for the most potent compound karanjin 7a.

Molecular docking studies

Molecular docking is an important computer aided tool to predict the binding interactions between best conformer of title compounds and protein (receptor) molecule to form stable complex.[17] This method helps researchers prioritize the most promising candidates of drug discovery.[17]

To understand the binding interactions of title compounds against receptor molecule, the docking simulations were performed against the crystal structure NADPH oxidase (PDB ID: 2CDU).[24] NADPH oxidase (NO) is chosen as an antioxidant drug target, because it is responsible for generation of reactive oxidation species. All newly synthesized title compounds recorded outstanding binding energy values compared to standard drug ascorbic acid. The docking scores are ranging from −7.9to −10.2 Kcal/mol and ascorbic acid scored −7.0 Kcal/mol only. The molecular docking scores and binding interactions of compounds 7a-d are presented in Figure 4 and Table 3.

Conclusion

In summary, an efficient, clean and convenient microwave assisted synthesis of karanjin derivatives. The procedure offers

several advantages including simple reaction conditions and product isolation procedures, thus, making the microwave synthesis of series of karanjin derivatives in good yields. The synthesized compounds were identified using IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. In addition, we have extracted karanjin from Pongamia pinnata seed. Both the extracted and synthesized compounds were subjected for antimicrobial activity. The SAR and biological activity results indicated that, the synthesized karanjin displayed a significant effect against bacteria and fungi over plant extracted karanjin. All the compounds 7a-d was screened for antioxidant activity by DPPH and hydrogen peroxide radical scavenging methods. The compound (7a-d) exhibited prominent IC_{50} value than standard drug ascorbic acid. Furthermore, that developed compounds showed promising antioxidant activity hence could be evaluated for their molecular docking studies. Insilco screening showed pretty good binding interactions and binding energies in comparison to reference and results are quite encouraging to extend research further.

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Conflict of interest statement

Authors declare there is no conflict of interest for this work.

Ethical declarations

No animals were used in this study.

References and Notes

1. D. J. Newman, G. M. Cragg, K. M. Snader, Natural products as sources of new drugs over the period 1981-2002, *J. Nat. Prod.* 2003, **66**, 1022-1037.
2. S. Brewer, The Relationship Between Natural Products and Synthetic Chemistry in the Discovery Process, *Spec. Pub. Royal Soc. Chem.* 2000, **257**, 59-65.
3. A. G. Atanasov, S. B. Zotchev, V. M. Dirsch, I. E. Orhan, M. Banach, J. M. Rollinger, Natural products in drug discovery: advances and opportunities. *Nat. Rev. Drug Discov.* 2021, **20**, 200-216.
4. A. Najmi, S. A. Javed, M. Al Bratty, H. A. Alhazmi, Modern approaches in the discovery and development of plant-based natural products and their analogues as potential therapeutic agents. *Molecules*, 2002, **27**, 349.
5. B. Meera, S. Kumar, S. B. Kalidhar, A review of the chemistry and biological activity of Pongamia pinnata. *J. Medicinal Aromatic Plant Sci.* 2003, **25**, 441-65.
6. B. J. Vinay, T. C. Sindhu Kanya, Effect of detoxification on the functional and nutritional quality of proteins of karanja seed meal, *Food Chem.* 2008, **106**, 77-84.
7. C. Muthu, M. Ayyanar, N. Raja, S. Ignacimuthu, Medicinal plants used by traditional healers in Kancheepuram district of Tamil Nadu, India. *J. Ethnobiol. Ethnomed.* 2006, **2**, 43.
8. M. U. Rehman, M. U. Rahman Mir, A. Farooq, S. M. Rashid, B. Ahmad, S. Bilal, Ahmad, R. Ali, I. Hussain, M. Masoodi, S. Mezzamil, H. Madkhali, M. Ahmad Ganaie Naringenin (4,5,7-trihydroxyflavanone) suppresses the development of precancerous lesions via controlling hyperproliferation and inflammation in the colon of Wistar rats, *Environ. Toxicol.*, 2018, **33**, 422-435.
9. S. A. Dahanukumar, R. A. Kulkarni, N. N. Rege, Pharmacology of medicinal plants and natural products, *Indian J. Pharmacol.* 2000, **32**, 81-118.
10. M. J. Rekha, B. K. Bettadaiah, S. P. Muthukumar, K. Govindaraju, Synthesis, characterization and anti-inflammatory properties of karanjin (Pongamia pinnata seed) and its derivatives. *Bioorganic Chemistry*, 2021, **106**, 104471.
11. S. Upadhyay, M. Dixit, Role of Polyphenols and Other Phytochemicals on Molecular Signaling, *Oxid. Med. Cell. Longev.* 2015, **2015**, 1-15.
12. B. S. Parmar, K. C. Gulati, Synergists for pyrethrins (II)-karanjin, *Indian J. Entomol.* 1969, **31**, 239-243.
13. P. V. Frank, B. Kalluraya, S. Shetty, Microwave Assisted Robinson's Annulation: Synthesis of some novel cyclohexenones under solvent free conditions, *Der Pharmacia Lettre*, 2011, **3(3)**, 388-392.
14. J. Xu, L. Zhang, Y. Liu, Synthesis and antioxidant activities of flavonoids derivatives, troxerutin and 3,4,7-triacetoxyethoxyquercetin, *Chinese Chem. Lett.* 2013, **24**, 223-226.
15. N. L. Naveena, T. R. Ravikumar Naik, Rudra Pratap, S.A. Shivashankar, Microwave assisted greener synthesis of silver nanoparticles using Karanjin and their antifungal activity, *J. Mater. NanoSci*, 5, **23**, 2018.
16. J. D. S. Costa, R. D. S. Ramos, K. D. S. L. Cuta, D. D. S. B. Brasil, C. H. T. D. P. D. Silva, E. F. B. Ferreira, R. D. S. Borges, J. M. Campos, W. J. D. C. Machdo, C. B. R. D. Santos, An In Silico Study of the Antioxidant Ability for Two Caffeine Analogs Using Molecular Docking and Quantum Chemical Methods. *Molecules*, 2018, **23**, 2801.
17. T. R. Ravikumar Naik, Therapeutic Significance of 1,4-Dihydropyridine Compounds as Potential Anticancer Agents, *Organic Synthesis-A Nascent Relook*. 2020, **1**, 217.
18. P. J. Bindu, T. R. Ravikumar Naik, S. Chandrashekar, K. M. Mahadevan. Synthesis, DNA binding, photocleavage, molecular docking studies of 2-oxo-3-quinoline-3-oximes. *J. Mol. Chem.* 2022, **2(2)**, 444.
19. P. J. Bindu, K. M. Mahadevan, N. D. Satyanarayan, T. R. Ravikumar Naik. Synthesis and DNA cleavage studies of novel quinoline oxime esters. *Bioorg. Med. Chem. Lett.* 2012, **22**, 898-900.
20. P. J. Bindu, K. M. Mahadevan, T. R. Ravikumar Naik. An efficient one-pot synthesis and photoinduced DNA cleavage studies of 2-chloro-3-(5-aryl-4,5-dihydroisoxazol-3-yl)quinolines. *Bioorg. Med. Chem. Lett.* 2012, **22(2)**, 6095-6098.
21. P. J. Bindu, K. M. Mahadevan, T. R. Ravikumar Naik. Sm(III)nitrate-catalyzed one-pot synthesis of furano[3,2c]-1,2,3,4-tetrahydroquinolines and DNA photocleavage studies. *J. Mol. Struct.* 2012, **1020**, 142-147.
22. P. J. Bindu, T. R. Ravikumar Naik, K. M. Mahadevan. Synthesis, DNA binding, docking and photocleavage studies of 2-chloro-3-quinolinyl-3-phenylpropen-2-ones. *Med. Chem. Comm*, 2014, **5**, 1708-1717.
23. T. R. Ravikumar Naik, S.A. Shivashankar, P.J. Bindu, In-vitro antioxidant and anticancer activities of $MnFe_2O_4$ nanoparticles synthesized using spinach leaves extract, *Appl. Nanomed.*, 2022, **22(1)**, 330.
24. B.R. Al Shammari, Antioxidant, Antimicrobial and In Silico NADPH Oxidase Inhibition of Chemically-Analyzed Essential Oils Derived from Ballota deserti (Noë) Jury, *Molecules*. 2022, **27(19)**, 6636.
25. R. J. Giguere, T. L. Bray, S. M. Duncan, G. Majetich, Application of commercial microwave ovens to organic synthesis, *Tetrahedron Lett.* 1986, **27**, 4945-4948.


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Microwave assisted nano $CuFe_2O_4$ catalyzed synthesis of 2,5-Diarylthiazoles and evaluation of their antioxidant activity supported by molecular docking studies

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Article



ABSTRACT

Reactive oxygen species play a significant role in various pathological conditions, searching for new antioxidants. While substituted phenols are known for their antioxidant properties, because of their limited stability and bioavailability are the present challenges for therapeutic applications. To address these limitations, we have developed a straightforward synthetic protocol of thiazole heterocycles. Microwave assisted heterogeneous nano $CuFe_2O_4$ catalyzed green and efficient method has been developed for the synthesis of 2,5-diarylthiazole derivatives. The chemical reaction of *N,N*-dimethyl-2-arylethen-1-amines with substituted benzothioamides in the presence of $CuFe_2O_4$ catalyst produced corresponding 2,5-diaryl substituted heterocycles in moderate-to-good yields. The synthesized compounds are confirmed by ^{1}H NMR, ^{13}C NMR, and mass spectra. The final compounds were evaluated for their in vitro antioxidant and molecular docking studies. The obtained thiazoles 3e, 3g and 3h showed the best antioxidant activities at IC_{50} =1.81 ± 0.12µg /mL, IC_{50} = 1.82 ± 0.12 µg /mL and IC_{50} = 1.67 ± 0.10 µg /mL for DPPH radicals respectively. Similary, 3e, 3g and 3h showed the best for Hydrogen peroxide scavenging activity. New compounds showed promising antioxidant activities having strong inhibitory activity. Moreover, molecular docking studies to evaluate the probable interactions with NADPH oxidase may provide new insights for developing these new sulfur heterocycles as potential antioxidant agents.

Keywords: Microwave irradiation, Nano $CuFe_2O_4$, Antioxidant, Molecular docking

INTRODUCTION

Thiazole ring is an important five-membered aromatic heterocyclic ring found in many natural compounds like vitamin B1-thiamine, alkaloids, flavones.[1-3] Few commercial drugs featuring the thiazole group in their core structure such as cefixime, dasatinib, nitazoxanide, meloxicam, abafungin and isavuconazole are widely employed in clinical antifungal treatments.[4] The interest in the synthesis of compounds containing the thiazole moiety has been increasing steadily in view of their diverse applications in the field of liquid crystals,[5,6] sensors,[7] sunscreens,[8] catalysts,[9] dyes[10] and chromophores.[11] Moreover, thiazole derivatives have various biological activities and are widely used in medicine. Thiazole and its derivatives shows their broad spectrum of activity like, antibacterial, antifungal, antimalarial, antitubercular, antiviral, anti-inflammatory, antidiabetic, anthelmintic, anticonvulsant, antioxidant, anticancer, and cardiovascular activities and known as new inhibitors of bacterial DNA gyrase B.[12]

Recently, heterogeneous nano catalysis in coupling reactions is a well-known topic in organic synthesis.[13] The application of magnetically reusable nanocatalysts in cross-coupling reactions to form carbon-carbon and carbon-heteroatom bonds has

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emerged as an extremely general technology for the preparation of a broad spectrum of drugs, biologically active molecules and mimics natural products.[16-25] Nowadays the catalytic potential of copper ferrite nanocatalysts was evaluated in a number of coupling reactions.[26-33]

On the other hand antioxidant activity plays an important role in the regulation of redox homeostasis and oxidative stress reduction.[34,35] Reactive oxygen species (ROS) generated during oxidation and rancidity of fats and oils are the main reason for oxidative damage, which causes cell or oxidative stress associated with many chronic diseases, like diabetes, cancer, and cardiovascular disorders. Small-molecule antioxidants containing sulfur can ameliorate oxidative damage, and cells employ multiple antioxidant mechanisms to prevent this cellular damage.[36,37] Thus, free radical scavenging has been suggested as potential therapeutic strategy for treatment of oxidative stress and inflammation-relative diseases.

Nowadays, molecular docking has been applied as a mechanistic tool to study the inhibition of enzymes that negatively affect antioxidant activity, like NADPH oxidase (NO), which is responsible for ROS generation.[38] One of the computational chemistry approaches, known as molecular docking, have recently gained great popularity in the field of modern drug development.[37] These approaches offer many benefits, notably enabling the analysis and interpretation of bioassay data, as well as effectively identifying potential drug targets and discovering new candidate drugs with enhanced therapeutic characteristics.[37] Molecular docking serves as one of the bioinformatics techniques that have been applied widely to explore the interactions between bioactive compounds and the active sites of specific proteins, with the aim of discovering the essential structural features that affect their binding efficiency.[37]

The large number of papers on the synthesis of biologically active 2,5-diarylthiazole that have appeared in recent years attests to the huge contemporary interest owing to its biodiversity. However, these previous methods faced some major limitations such as expensive materials, extreme heating, tedious intermediate preparation, lower yields, harsh conditions etc. It is noteworthy that a convenient and cost-effective approach is still in demand to develop these scaffolds in terms of better yields, large-scale synthesis and inexpensive auxiliaries. In the continuation of our ongoing research, we are delighted to introduce an $CuFe_2O_4$ MNPs catalyzed alternative synthetic strategy to achieve novel 2,5-diarylthiazole analogues. Taking inspiration from the above and as a part of our continuing research on the synthesis and biologically activity of fused heterocyles.[38-42] Therefore, there is a need to develop new antioxidants capable of preventing oxidative damage by interacting with free radicals or inhibiting their activity. In this perspective, we describe the synthesis of medicinal important 2,5-diarylthiazole (Scheme 1) and studied their molecular docking studies.

Materials and Methods

All the chemicals used in the present study are of AR grade. M/s Sigma-Aldrich, and Merck, USA and M/s S.D. Fine Chem. Pvt. Ltd, Mumbai, India. Melting points were recorded on an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analyses were carried out using a Perkin-Elmer 240C CHN analyzer. IR spectra were recorded on a FT-IR infrared spectrophotometer. 1H-NMR spectra were obtained using 300 MHz and 400 MHz on a Bruker spectrometer (chemical shifts in δ ppm). Mass spectra were recorded using a micro spray Q-TOF MS ES Mass spectrometer.

In vitro antioxidant activity of 2,5-diarylthiazoles.

As a continuation of our previous work on [illegible] activity [43] of wide variety of heterocyclic syste[illegible] we aimed to design and construct 2,5-diarylthia[illegible] from relatively simple starting materials.

Molecular Docking Protocol

In present study, Autodock was used.[37] Auto[illegible] empirical scoring function to calculate binding energy of protein-drug molecule.[37] The crystal structure of NADPH oxidase (PDB ID: 2CDU).[41] was downloaded from Protein Data Bank. Initially, the macromolecule was prepared by removing water molecules and hetero atoms, polar hydrogens were added. In-house synthesized drug molecules were drawn in MDL file (.mol) format using Chemsketch. After docking, conformations were ranked according to their binding energy, and the confirmation with the lowest binding energy was considered as the best docking score. The docking results were visualized using Pymol Visualizer.[37]

Experimental

General procedure for the synthesis of 2,5-diarylthiazoles (2a):

A mixture of N,N-dimethyl-2-arylethen-1-amines (10 mmol) was dissolved in anhydrous DMSO (15 mL) and stirred for 10 minutes at room temperature. Add substituted benzothioamides (10 mmol), $CuFe_2O_4$ (30 mg) and Cs_2CO_3 (2 equiv, 20 mmol) under an N2 atmosphere to the reaction mixture was stirred for 10 min. After completion of addition, the reaction mixture was transfer in 100 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 40 minutes. The completion of the reaction was confiremed by TLC and it was allowed to cool to room temperature. The reaction mixture was quenched with saturated salt water (30 mL), and the solution was extracted with ethyl acetate (3×30 mL). The solvent was removed under reduced pressure using a rotary evaporator. The structures of all the synthesized molecules were established by spectral analyses (^{1}H NMR, ^{13}C NMR, and mass) data. All the synthesized compounds showed appropriate characteristic signals, which confirm their structures.

The desired product **2,5-diphenylthiazole (3a)**: Yellow solid, m.p. 117-119 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.0 (d, 2H, J = 7.6 Hz), 7.8 (d, 2H, J = 7.6 Hz), 7.4 (m, 6H), 7.3 (t, 1H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ =161, 150, 131, 129, 128, 128, 127, 127, 126, 124, 123; HRMS(ESI): m/z calcd for $C_{15}H_{11}NSNa$ (M+Na)+: 260.0319, found: 260.0317.

5-phenyl-2-(p-tolyl)thiazole (3b): Yellow solid, m.p. 118-120 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.0 (d, 2H, J = 7.6 Hz), 7.7 (d, 2H, J = 7.6 Hz), 7.5 (t, 3H, J = 7.4 Hz), 7.4 (d, 1H, J = 7.6

Hz), 7.3 (d, 2H, J = 8.0 Hz), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162, 151, 141, 130, 129, 128, 128, 126, 124, 124, 123, 23; HRMS(ESI): m/z calcd for $C_{16}H_{13}NSNa$ (M+Na)+: 274.0346, found: 274.0344.

2-(4-chlorophenyl)-5-phenylthiazole (3c): Yellow solid, m.p. 122-℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.0 (d, 2H, J = 7.6 Hz), 7.8 (d, 2H, J = 7.6 Hz), 7.6 (m, 5H), 7.4 (t, 1H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=160, 153, 138, 130, 128, 128, 127, 127, 124, 124, 123; HRMS(ESI): m/z calcd for $C_{15}H_{10}ClNSNa$ (M+Na)+: 294.0764, found: 294.0762.

2-(4-bromophenyl)-5-phenylthiazole (3d): Yellow solid, m.p. 121-123 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.1 (d, 2H, J = 7.6 Hz), 7.7 (d, 2H, J = 7.6 Hz), 7.6 (d, 2H, J = 8.8 Hz), 7.4 (m, 3H), 7.3 (t, 1H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=172, 161, 152, 130, 129, 128, 127, 126, 126, 124, 124, 123; HRMS(ESI): m/z calcd for $C_{15}H_{10}BrNSNa$ (M+Na)+: 337.0215, found: 337.0213.

2-(4-methoxyphenyl)-5-phenylthiazole (3e): Yellow solid, m.p. 108-110 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.9 (t, 3H, J = 7.4 Hz), 7.6 (s, 1H), 7.4 (m, 5H), 7.0 (q, 1H, J = 4.2 Hz), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162, 159, 150, 129, 129, 128, 128, 128, 124, 123, 118, 116, 112, 56; HRMS(ESI): m/z calcd for $C_{16}H_{13}NOSNa$ (M+Na)+: 290.0616, found: 290.0614.

2-(4-nitrophenyl)-5-phenylthiazole (3f): Yellow solid, m.p. 210-212 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.4 (d, 2H, J = 7.6 Hz), 8.0 (m, 2H), 7.8 (d, 2H, J = 7.6 Hz), 7.6 (s, 1H), 7.5 (t, 3H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162, 150, 148, 134, 132, 129, 126, 126, 126, 124, 124; HRMS(ESI): m/z calcd for $C_{15}H_{10}N_2O_2SNa$ (M+Na)+: 305.0317, found: 305.0315.

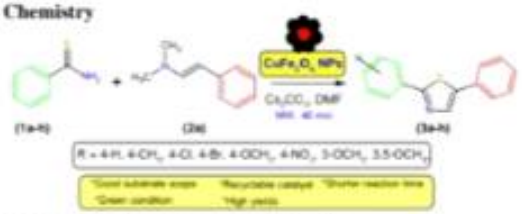
2-(3-methoxyphenyl)-5-phenylthiazole (3g): Yellow solid, m.p. 123-125 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.9 (t, 2H, J = 7.6 Hz), 7.7 (s, 1H), 7.3 (m, 5H), 7.0 (q, 1H, J = 8.4 Hz), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162, 160, 152, 130, 128, 128, 128, 128, 124, 123, 118, 118, 116, 55; HRMS(ESI): m/z calcd for $C_{16}H_{13}NOSNa$ (M+Na)+: 290.0345, found: 290.0343.

2-(3,5-dimethoxyphenyl)-5-phenylthiazole (3h): Yellow solid, m.p. 128-130 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.8 (t, 2H, J = 7.6 Hz), 7.6 (s, 1H), 7.4 (m, 5H), 7.0 (q, 1H, J = 8.4 Hz), 3.86 (s, 3H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162, 159, 152, 130, 129, 129, 128, 128, 124, 123, 118, 116, 114, 56, 55; HRMS(ESI): m/z calcd for $C_{17}H_{15}NO_2SNa$ (M+Na)+: 320.0715, found: 320.0713.

Results and Discussion

Recently, the large number of papers on the synthesis of Sulfur-containing heterocyclic compounds that have appeared in recent years attests to the huge contemporary interest owing to its biodiversity. Free radicals are not only closely related to human aging, but also deeply involved in the occurrence, development and treatment of human diseases. The response to excess free radicals in body is usually characterized with oxidative stress and inflammation. With these precedents in mind, in this work we have designed and synthesized thiochromenes (Scheme 1, Table 1) and investigated their antioxidant property and molecular docking studies.

Chemistry



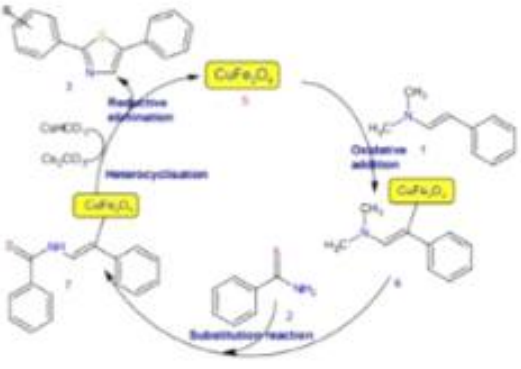
Scheme 1: Synthesis of 2,5-diarylthiazoles.

Table 1. Scope of 2,5-diarylthiazole and its derivatives

Products[a]	R	Time (min)	Yield(%)[b]	M.P. (°C)
3a	H	40	90	117-119
3b	4-CH_3	40	90	118-120
3c	4-Cl	40	85	122-124
3d	4-Br	40	85	121-123
3e	4-OCH_3	40	92	108-110
3f	4-NO_2	40	85	210-212
3g	3-OCH_3	40	90	123-125
3h	3,5-OCH_3	40	90	128-130

[a]All the products were characterized by elemental analysis,^{1}H NMR, ^{13}C NMR and Mass spectral studies. [b]Yields of isolated products.

The synthesis of title compounds is shown in Scheme-1, Table-1. The reaction conditions were screened based on the model reaction involving benzothioamide and N,N-dimethyl-2-phenylethen-1-aminethiophenol. $CuFe_2O_4$ was employed as a bifunctional catalyst, with surface Cu^{2+} and Fe^{3+} centers capable of activating N,N-dimethyl-2-phenylethen-1-aminethiophenol, stabilizing intermediates, and promoting the Lewis acid-driven rearrangement. Cs_2CO_3 was chosen as a mild, soluble base compatible with the catalytic system and the reaction was performed in DMSO, a thermally robust and chemically suitable solvent. The $CuFe_2O_4$ NPs which were proven to efficient catalyst for the C-S coupling reactions shown in Scheme 1.



Scheme 2: $CuFe_2O_4$ NPs catalyzed mechanism for the synthesis of 2,5-diarylthiazoles

Plausible mechanism to account for the reaction is shown in Scheme 2. The N,N-dimethyl-2-phenylethen-1-aminethiophenol

(1) coordinate with $CuFe_2O_4$ NPs (5) a corresponding intermediate (6) was generated by an oxidative addition step. Next, the intermediate (6) reacted with benzothioamide (2) to produce a intermediate N,N-dimethyl-2-arylethen-1-amine (7). Finally, the intermediate (7) generates the desired product (3) by heterocyclization and a reductive elimination step. The $CuFe_2O_4$ NPs removed by external bar magnet and reused further.

Table 2. Binding affinities and Druglikeness of 2,5-diarylthiazoles with amino acids of NADPH oxidase (PDB ID: 2CDU).

SLNo	miLogP	TPSA	n_{atoms}	MolLogS	Drug-Score	Binding Energy (Kcal/mol)
3a	4.71	12.89	17	-4.60	-1.22	−10.0
3b	5.16	12.89	18	-5.31	-0.95	−10.0
3c	5.36	12.86	18	-6.05	-0.69	−7.8
3d	5.51	12.89	18	-5.36	-1.13	−8.0
3e	4.76	22.13	19	-4.66	-0.90	−9.2
3f	4.67	58.72	20	-3.70	-0.73	−8.1
3g	4.71	22.13	19	-4.51	-1.26	−9.1
3h	4.75	31.36	21	-4.54	-1.33	−9.3

This approach addresses the synthetic and environmental limitations of previous methods delivers good yields across a broad substrate scope and employs a magnetically separable catalyst that retains high activity over five consecutive cycles without significant loss of efficiency. Hence, the work presented herein demonstrates the utility of this strategy and evaluates its potential as a more sustainable and broadly applicable method for the synthesis of thiazoles.

Biological Activity

The application of computational tools in drug discovery has become increasingly critical due to their efficiency in screening and evaluating large libraries of chemical compounds. Molinspiration is one such tool that provides researchers with the ability to perform rapid molecular property calculations and bioactivity predictions. Hence we calculated Druglikeness properties like miLogP, TPSA, Drug-Score of 2,5-diarylthiazoles (Table-2).

In vitro antioxidant activity of 2,5-diarylthiazoles.

As explained in the introduction section, free radicals have aroused significant interest among scientists in the past decade. Their broad range of effects in biological system has drawn the attention of many experimental works. It has been proved that these mechanisms may be important in the pathogenesis of certain diseases and ageing. There are many reports that support the use of antioxidant supplementation in reducing the level of oxidative stress and in slowing or preventing the development of complications associated with diseases.

DPPH radical scavenging activity

DPPH, a stable free radical at room temperature, which produces a purple colour solution in methanol. It is reduced in the presence of synthesized antioxidant molecule, giving rise to uncoloured methanol solutions. The DPPH has a strong absorption at 517 nm and upon reduction by a free radical scavenging antioxidant, this absorption is decreased. We found that they exhibited free radical scavenging activity against the stable free radical DPPH. Figure 1 and Table 3. All compounds 3a-3h expressed significant IC_{50} values for DPPH radicals. Compound 3e IC_{50} 1.81 ± 0.12μg /mL, 3g IC_{50} 1.82 ± 0.12 μg /mL and 3h is IC_{50} 1.67 ± 0.10 μg /mL for DPPH radicals respectively as shown in Table 3. The inhibitory activity gets higher depends on substitutions and presence of alkoxy group in thiazole 3e, 3g and 3h compared to other derivatives.[44]

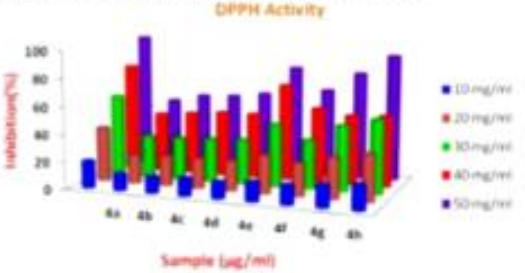


Figure 1. DPPH radical scavenging activity of 2,5-diarylthiazoles (3a-h).

Hydrogen peroxide (H_2O_2) scavenging activity

H_2O_2 is freely diffusible across membranes and thus may cause oxidative stress in neighboring cells. Quenching of H_2O_2 increases as the concentration increases with the decrease of absorbance at 420 nm. The compounds 3c, 3g, and 3h showed good H_2O_2 inhibition compared to standard antioxidant Ascorbic acid. 3e IC_{50} 11.80 ± 0.10μg /mL, 3g IC_{50} 1.85 ± 0.12 μg /mL and 3h is IC_{50} 1.71 ± 0.10 μg /mL higher than Ascorbic as shown in Figure 2 and Table 3.[44]

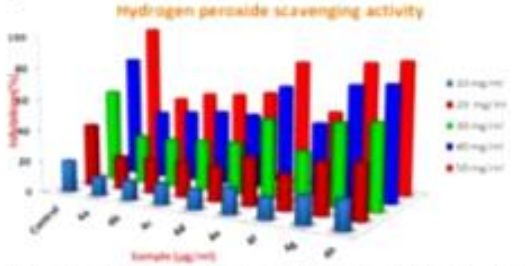


Figure 2. Hydrogen peroxide scavenging activity of 2,5-diarylthiazoles (3a-h).

Table 3. Antioxidant activity of Target Compounds (3a-h).

Entry[a]	DPPH Method Percentage of inhibition	IC_{50} value	H_2O_2 Method	IC_{50} value
3a	32.41	3.86 ± 0.12	35.92	4.15 ± 0.25
3b	36.58	3.18 ± 0.31	41.25	*4.58 ± 0.12*
3c	48.24	5.04 ± 0.28	44.68	5.27 ± 0.12
3d	50.01	5.48 ± 0.12	48.21	6.18 ± 0.12
3e	72.16	1.81 ± 0.12	79.89	1.80 ± 0.10
3f	48.31	5.36 ± 0.12	47.60	6.89 ± 0.12
3g	70.90	1.82 ± 0.12	81.28	1.85 ± 0.12
3h	75.25	1.67 ± 0.10	*84.82*	1.71 ± 0.10
Ascorbic acid	70.82	1.95 ± 0.10	78.19	1.80 ± 0.12

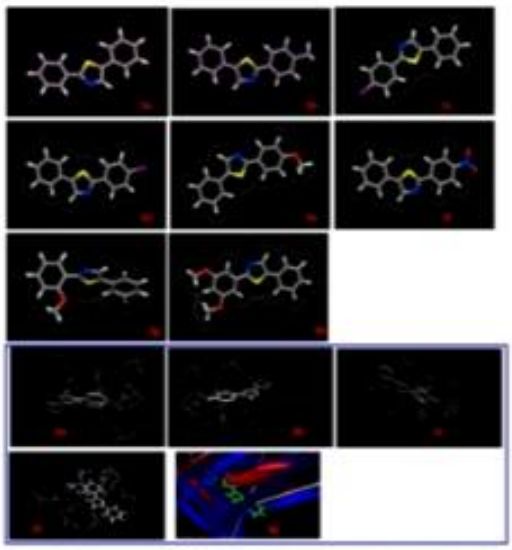


Figure 3. Molecular docking and 3D electron cloud studies of 2,5-diarylthiazoles (3a-h).

SAR studies showed that 2,5-diarylthiazoles nuclei at the position of 2 and 3 with specific hydrophilic groups increased activity compared to other hydrophobic groups. Antioxidant activity of 2,5-diarylthiazoles is performed by DPPH and Hydrogen Peroxide radical scavenging methods taking Ascorbic acid as reference. Antioxidant activity is expressed as Percentage of inhibition. Compounds (3e, 3g and 3h in Figure 2) exerted enhanced activity in comparison to standard drug. Structural activity relations observation demonstrates antioxidant activity depends on electronic factor of substituent aromatic benzene ring. Incorporation of electron releasing substituent at para-position improved activity compared to unsubstituted analogue. Introduction of electron withdrawing substituent at para-position lowers activity. Antioxidant activity of synthesized compounds and IC_{50} values of synthesized compounds are presented in Table 3. Target compound showed excellent antioxidant activity.[44]

Molecular docking studies

Molecular docking is an important computer aided tool to predict the binding interactions between best conformer of title compounds and protein (receptor) molecule to form stable complex.[37] This method helps researchers prioritize the most promising candidates of drug discovery.[37,43]

To understand the binding interactions of title compounds against receptor molecule, the docking simulations were performed against the crystal structure NADPH oxidase (PDB ID: 2CDU).[44] NADPH oxidase (NO) is chosen as an antioxidant drug target, because it is responsible for generation of reactive oxidation species. All newly synthesized title compounds recorded outstanding binding energy values compared to standard drug ascorbic acid. The docking scores are ranging from −7.8 to −10.0 Kcal/mol and ascorbic acid scored −6.7 Kcal/mol only. The molecular docking scores and binding interactions of compounds (3a-h) are presented in Figure 1 and Table 1.

In Figure 1, the green color represents the 3D structure of thiazole 3f, the blue dashed line represents hydrogen bonding, and the gray dashed line represents the hydrophobic interaction. Thus, we could see that compound 3f is embedded into the protein crystal structure NADPH oxidase. The binding interactions of compounds at active sites amino acids of NADPH oxidase are matching to the interactions of ascorbic acid with many compounds. The standard compound ascorbic acid confirmed H-bond interactions with amino acids in cavity of NADPH oxidase (Fig. 2). The docking scores and binding interactions prove that these molecules could best fit into the pocket of NADPH oxidase.

Conclusion

In conclusion, we described the microwave assisted CuFe2O4 NPs catalyzed synthesis, antioxidant activity and molecular docking studies of 2,5-diarylthiazole derivatives. The $CuFe_2O_4$ NPs was employed as a bifunctional catalyst, with surface Cu^{2+} and Fe^{3+} centers capable of C-S coupling reactions. This heterogeneous catalyst efficiency is achieved in several aspects, such as high product yields and reactivity in a green manner, stability, recyclability, and high reaction rate. Furthermore, the easy separation and removal from the reaction make this catalyst a good choice for use in other synthetic applications. These results affirmed that the novel $CuFe_2O_4$ can be used as a versatile catalyst for promoting chemical reactions. This new methodology provides an efficient and economical approach toward 2,5-diarylthiazole derivatives. The synthesized compounds evaluated for their antioxidant activity and molecular docking studies. The synthesized compounds 3e, 3f, and 3h showed good activity against the tested antioxidants. The alkoxy substituted 2,5-diarylthiazoles showed healthy antioxidant activity compare to other derivatives, hence we evaluated for their molecular docking studies. Insilco screening showed pretty good binding interactions and binding energies in comparison to reference. Findings reveal that, the versatile scaffolds results in enhanced biological activity and provides scope for further research.

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Conflict of interest statement

Authors declare there is no conflict of interest for this work.

Ethical declarations

No animals were used in this study.

References and Notes

1. Z. Hongyun, Z. Jun'gan, H. Wei. New Method for the Synthesis of 2,5-Diaryl Substituted Thiazoles. *Chin. J. Org. Chem.* **2020**, 40(8), 2535-2542.
2. A. Parthasarathy, E. J. Borrego, M. A. Savka, R. C. Dobson, A. O. Hudson. Amino acid-derived defense metabolites from plants: A potential source to facilitate novel antimicrobial development. *J. Biol. Chem.* **2021**, 296, 100438.
3. Sara M. Mostafa, Ashraf A. Aly, Stefan Bräse, Martin Nieger, Asmaa H. Mohamed. *J. Sulfur Chem.* **2022**, 43, 606-619.

4. D. Gao, L. Shi, Y. Huang, Y. Lv, X. Yang, Z. Du, Synthesis of 2-Amino-4,5-Diarylthiazole Derivatives and Evaluation of Their Anti-Candida Albicans Activity, *Molecules*, **2025**, 30(7), 1643.
5. A. Kiryanov, P. Sampson, A. J. Seed. Synthesis of 2-alkoxysubstituted thiophenes, 1,3-thiazoles, and related S-heterocycles via Lawesson's reagent-mediated cyclization under microwave irradiation. Applications for liquid crystal synthesis. *J. Org. Chem*, **2001**, 66, 7925.
6. A. Mori, A. Sekiguchi, K. Masui, T. Shimada, M. Horie, K. Osakada. Facile synthesis of 2,5-diarylthiazoles via palladium-catalyzed tandem C–H substitutions. Design of tunable light emission and liquid crystalline characteristics. *J. Am. Chem. Soc*, **2003**, 125, 1700.
7. B.-Y. Kim, H.-S. Kim and A. Helal, A fluorescent chemosensor for sequential recognition of gallium and hydrogen sulfate ions based on a new phenylthiazole derivative. *Sens. Actuators, B*, **2015**, 206, 430-434.
8. T. Bach, S. Heuser. Synthesis of 2-(o-hydroxyaryl)-4-arylthiazoles by regioselective Pd(0)-catalyzed cross-coupling. *Tetrahedron Lett.*, **2000**, 41, 1707.
9. A. Dondoni. Heterocycles in organic synthesis: Thiazoles and triazoles as exemplar cases of synthetic auxiliaries. *Org. Biomol. Chem*, **2010**, 8, 3366-3385.
10. M. A. Metwally, E. Abdel-Latif, F. A. Amer, G. Kaupp. Synthesis of new 5-thiazolyl azo-disperse dyes for dyeing polyester fabrics. *Dyes Pigm*, **2004**, 60(3), 249-264.
11. X. G. Guo, J. Quinn, Z. H. Chen, H. Usta, Y. Zheng, Y. Xia. Dialkoxybithiazole: A New building block for head-to-head polymer semiconductors. *J. Am. Chem. Soc*, **2013**, 135, 1986-1996.
12. K. H. Narasimhamurthy, T. R. Swarup, K. S. Rangappa. A review on progress of thiazole derivatives as potential anti-inflammatory agents. *Eur. J. Med. Chem*, **2024**, 12, 100225.
13. D. A. Waad, E. H. Mahmoud, M. M. Shaheeda, A. Abdulmalik, S. Hussein, E. H. El-Sayed. Antibacterial, antibiofilm and molecular modeling study of some antitumor thiazole based chalcones as a new class of DHFR inhibitors. *Microb. Pathog*, **2019**, 136, 103674.
14. T. R. Ravikumar Naik, S. A. Shivashankar. Heterogeneous bimetallic $ZnFe_2O_4$ nanopowder catalyzed synthesis of Hantzsch 1,4-dihydropyridines in water. *Tetrahedron Lett*, **2016**, 57, 4046-4049.
15. J. Wang, S. A. Lee, H. W. Jang, M. Shokouhimehr. Emerging Two-Dimensional-Based Nanostructured Catalysts: Applications in Sustainable Organic Transformations. *Langmuir*, **2022**, 38, 9064-9072.
16. M. Nasrollahzadeh, N. Motahharifar, M. Sajjadi, A. Naserimanesh, M. Shokouhimehr. Functionalization of chitosan by grafting Cu(II)-5-amino-1H-tetrazole complex as a magnetically recyclable catalyst for C-N coupling reaction. *Inorg. Chem. Commun.*, **2022**, 136, 109135.
17. K. H. Chen, M. Shokouhimehr, Y. E. Sung. Heterogeneous Suzuki Cross-Coupling Reaction Catalyzed by Magnetically Recyclable Nanocatalyst. *Bull. Korean Chem. Soc.*, **2013**, 34, 1477-1480.
18. Monfared, R. Mohammadi, S. Ahmadi, M. Nikpassand, A. Hosseinian. Recent advances in the application of nano-catalysts for Heyana cross-coupling reactions. *RSC Adv*, **2019**, 9, 3185-3202.
19. H. Veisi, B. Karmakar, P. Mohammadi, T. Tamoradi, S. Hemmati, Z. Joshani. metal catalyst supported on modified carbon nano tubes (CNTs) for cross-coupling reactions. *Inorg. Chem. Commun*, **2023**, 156, 110979.
20. R.Tandon, N. Tandon, S. M. Patil. Overview on magnetically recyclable ferrite nanoparticles: synthesis and their applications in coupling and multicomponent reactions. *RSC Adv*, **2021**, 11, 29333-29353.
21. J. W. Meringdal, D. Menche. Suzuki–Miyaura (hetero-) Aryl cross-coupling: recent findings and recommendations. *Chem. Soc. Rev.*, **2025**, 54, 5746–5765.
22. L. Chen, S. Rangan, J. Li, H. Jiang, Y. Li. A molecular Pd (II) complex incorporated into a MOF as a highly active single-site heterogeneous catalyst for C-Cl bond activation. *Green Chem*, **2014**, 16, 3978-3985.
23. S. J. Hoseini, V. Heidari, H. Nasrabadi. Magnetic Pd/Fe_3O_4 reduced-graphene oxide nanohybrid as an efficient and recoverable catalyst for Suzuki–Miyaura coupling reaction in water. *J. Mol. Catal. Chem*, **2015**, 396, 90-95.
24. J. Liu, H. Zhan, N. Wang, Y. Song, C. Wang, X. Wang, L. Ma, L. Chen. Palladium nanoparticles on covalent organic framework supports as catalysts for Suzuki–Miyaura cross-coupling reactions. *ACS Appl. Nano Mater*, **2021**, 4, 6279-6249.
25. A. Sathya, T. R. Ravindran, J. Philip. Superior thermal stability of polymer capped Fe_3O_4 magnetic nanoclusters. *J. Am. Ceram. Soc*, **2018**, 101, 485-491.
26. R. Veligeti, J. S. Anireddy, R. B. Madhu, A. Bendi, P. L. Praveen, D. S. Ramakrishna. Solvent-free synthesis of acridone based dihydropyrazine derivatives using $CuFe_2O_4$ nanoparticles as heterogeneous catalyst: molecular docking and in-vitro studies as anticancer agents. *J. Inorg. Organomet. Polym. Mater*, **2023**, 33, 4039-4051.
27. A.K. Raigar, Manju, K. Saini, A. Galeria, $CuFe_2O_4$-catalyzed one-pot synthesis of α-substituted 2-benzofuranmethanimines via tandem A3 coupling, 5-exo-dig cyclization, and 1,3-allylic rearrangement, *RSC Adv.*, **2025**,15, 32108-32116.
28. G. Satish, K. H. V. Reddy, K. Ramesh, B. S. P. A. Kumar, Y. V. D. Nageswar, An elegant protocol for the synthesis of N-substituted pyrroles through C–N cross coupling aromatization process using $CuFe_2O_4$ nanoparticles as catalyst under ligand-free conditions, *Tetrahedron Lett*, **2014**, 55 , 2596-2599.
29. A.R. Hajipour, M. Karimzadeh, G. Azizi, Highly efficient and magnetically separable nano-$CuFe_2O_4$ catalyzed S-arylation of thiourea by aryl/heteroaryl halides, *Chin. Chem. Lett*, **2014**, 25, 1382-1386.
30. G. Satish, K. H. V. Reddy, B. S. P. Anil, K. Ramesh, R. U. Kumar, Y. V. D. Nageswar, Direct C–H arylation of benzothiazoles by magnetically separable nano copper ferrite, a recyclable catalyst, *Tetrahedron Lett*, **2015**, 56, 4950.
31. M. Ghobadi Based on copper ferrite nanoparticles ($CuFe_2O_4$): catalysis in synthesis of heterocycles. *J. Synth. Chem*, 2022, 1, 84-96.
32. S. Sharma, P. Iakhar and H. Sharma, $CuFe_2O_4$ nanomaterials: current discoveries in synthesis, catalytic efficiency in coupling reactions, and their environmental applications, *J. Chin. Chem. Soc.*, **2023**, 70, 107-127.
33. D. Sanap, L. Avhad, S. Ahire, M. Mirzaei, D. Kumar, S. Ghotekar, N. D. Gaikwad, Insights into the promising heterogeneous catalysis of eco-friendly synthesized spinel $CuFe_2O_4$ nanoparticles for Biginelli reaction, *Res. Chem. Intermed*, **2024**, 50, 3687-3711.
34. S. Reuter, S. C. Gupta, M. M. Chaturvedi, B. B. Aggarwal, Oxidative stress, inflammation, and cancer: how are they linked?, *Free Radic. Biol. Med*, **2010**, 49, 1603-1616.
35. E. E. Battin, J. L. Brumaghim, Antioxidant activity of sulfur and selenium: a review of reactive oxygen species scavenging, glutathione peroxidase, and metal-binding antioxidant mechanisms, *Cell Biochem Biophys*, **2009**, 55(1), 1-23.
36. J. D. S. Costa, R. D. S. Ramos, K. D. S. L, Cota et.al. An in silico study of the antioxidant ability for two caffeine analogs using molecular docking and quantum chemical methods. *Molecules*, **2018**, 23, 2803.
37. T. R. Ravikumar Naik, Therapeutic Significance of 1,4-Dihydropyridine Compounds as Potential Anticancer Agents, *Organic Synthesis-A Nascent Relook*, **2020**, 1, 217.
38. P. J. Bindu, T. R. Ravikumar Naik, S. Chandrashekar, K. M. Mahadevan. Synthesis, DNA binding, photocleavage, molecular docking stuies of 2-exo-3-quinoline-3-oximes. *J. Mol. Chem*, **2022**, 2(2), 444.
39. P. J. Bindu, K. M. Mahadevan, N. D. Satyanarayan, T. R. Ravikumar Naik. Synthesis and DNA cleavage studies of novel quinoline oxime esters. *Bioorg. Med. Chem. Lett*, **2012**, 22, 898-900.
40. P. J. Bindu, K. M. Mahadevan, T. R. Ravikumar Naik. An efficient one-pot synthesis and photoinduced DNA cleavage studies of 2-chloro-3-(5-aryl-4,5-dihydroisoxazol-3-yl)quinolines. *Bioorg. Med. Chem. Lett*, **2012**, 22(2), 6095.
41. P. J. Bindu, K. M. Mahadevan, T. R. Ravikumar Naik. $Sm(III)$nitrate-catalyzed one-pot synthesis of furano[3,2c]-1,2,3,4-tetrahydroquinolines and DNA photocleavage studies. *J. Mol. Struct*, **2012**, 1020, 142-147.
42. P.J. Bindu, T.R. Ravikumar Naik, G. Krishnamurthy. Synthesis, DNA binding and molecular docking studies of 2H-benzo[b][1,4] oxazines, *Biomed. Ther. Lett*, **2025**, 12(1), 1153.
43. T. R. Ravikumar Naik, P. J. Bindu. Antimicrobial, antioxidant and molecular docking studies of Karanja derivatives synthesized via Microwave assisted synthesis, *Biomed. Ther. Lett*, **2026**, 13(1), 1852-1859.
44. P. J. Bindu, T. R. Ravikumar Naik, K. M. Mahadevan. Synthesis, DNA binding, docking and photocleavage studies of 2-chloro-3-quinolinyl-3-phenylpropen-2-ones, *Med. Chem. Comm*, **2014**, 5, 1708-1717.

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6(2), 1711

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$CuFe_2O_4$ nanocatalysed one-pot microwave-assisted synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones and their antioxidant activity

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ABSTRACT

A facile and greener synthetic microwave assisted method has been developed for the synthesis of 2-aryl-2,3-dihydroquinoli-4(1H)-ones from 2-aminoacetophenone and substituted benzaldehydes using nano $CuFe_2O_4$ catalyst under mild reaction condition. This synthetic protocol provides rapid access to a variety of 2-aryl-2,3-dihydroquinolin-4(1H)-ones. This technique has several advantages, such as the use of easily available starting materials, the efficiency of the catalyst, a simple operation, and tolerance of a wide range of functionality in the aldehydes. All the compounds (3a-g) were screened for antioxidant activity by DPPH methods. The 2-aryl-2,3-dihydroquinolin-4(1H)-ones (3a-g) exhibited prominent IC_{50} value than standard drug ascorbic acid.



Keywords: *$CuFe_2O_4$ Bimetallic catalyst, Microwave irradiation, 2-Aryl-2,3-dihydroquinolin-4(1H)-ones, Antioxidant*

INTRODUCTION

Microwave-Assisted Organic Synthesis (MAOS) has emerged as a revolutionary approach in green chemistry, offering an energy-efficient, environmentally friendly alternative to traditional synthetic methods.[1,2] Traditional organic synthesis faces challenges such as excessive reaction times, high solvent consumption, and significant chemical waste. Microwave irradiation enhances reaction efficiency by selectively heating the reaction mixture, leading to faster reaction rates, improved yields, and reduced byproduct formation. This technique aligns with the principles of green chemistry by minimizing toxic solvent use and optimizing reaction conditions for sustainability.[1,2]

Metal Nanoparticles are widely used catalysts in organic synthesis due to their adjustable size, shape-associated activity and selectivity. In particular, magnetic bimetallic catalysts are more advantageous than mono catalysts due to variations in their electronic configuration, surface composition and oxidation states.[3-10] The resulting synergistic effect can enhance the catalytic activity, selectivity and stability of magnetic bimetallic catalysts. The $CuFe_2O_4$ catalysts are more promising due to their greater abundance, low cost, improved catalytic activity and stability in organic synthesis.[3-10]

Recently, one of the intentions of medicinal chemistry research and drug discovery is to develop compounds that show desirable biological activities and easily accessible. Such compounds should be either isolated from natural resources or synthesized in the laboratory. The time and resources required to bring such biologically active compounds to the market can be minimized.[11] The flavanones and 2-aryl-2,3-dihydroquinolin-4(1H)-ones both are naturally occurring compounds belonging to the flavonoid family and are valuable precursors in the synthesis of flavones.[12] The 2-aryl-2,3-dihydroquinolin-4(1H)-ones are valuable precursors in the synthesis of quinolin-4(1H)-ones,[13] 4-alkoxy-2-aryl quinolines, 2-aryl-4-quinolones, and 3-aryl-4-quinolones.[14-16]

The large number of articles on the synthesis of 2,3-dihydroquinolin-4(1H)-one that have appeared in recent years attests to the huge contemporary interest owing to its usefulness. The construction of 2,3-dihydroquinolin-4(1H)-ones based on intra- and intermolecular cyclization of 2-aminochalcones under different reaction conditions, like antimony(III) chloride,[17]

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ytterbium(III) triflate,[19] indium(III) chloride,[19] zinc chloride,[20] phosphorous acid,[21] phosphomolybdic acid–silica gel,[22] silica gel supported sodium bisulfite,[23] silica gel supported tantalum(V) bromide,[24] silica chloride with microwave irradiation,[25] PEG-400,[26] alumina-supported cerium(III) chloride heptahydrate–sodium iodide,[27] piperidine with potassium hydroxide,[28] sodium ethoxide,[29] and ionic liquids.[30]

Considering the significance of 2-aryl-2,3-dihydroquinolin-4(1H)-ones, their synthesis is still in demand by organic researchers and nowadays, greener methodologies are being considered. However, most of the earlier published techniques have at least one of the following drawbacks: corrosive reagents like acids, or strong alkalis, low yields, long reaction time and large amount of catalyst or solvent used, laborious workup, hazardous catalysts used and difficult reaction assemblage etc. It is noteworthy that a convenient and cost-effective approach is still in demand to develop these scaffolds in terms of better yields, large-scale synthesis and inexpensive auxiliaries.

In continuation of our effort to tap the barely exploited potential of $CuFe_2O_4$ nano particles in organic synthesis, we report herein the use of $CuFe_2O_4$ bimetallic catalyst for the efficient synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones. Taking inspiration from the above and as a part of our continuing research on the synthesis of biologically active compounds.[31-35] Hence, the need to be replaced by newer drugs periodically. From this perspective, we describe the microwave assisted $CuFe_2O_4$ nano particles catalyzed one-pot synthesis of the pharmacologically important 2-aryl-2,3-dihydroquinolin-4(1H)-ones (Scheme 1). In addition, we also report the DPPH antioxidant activities of the synthesized 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

MATERIALS AND METHODS

All the chemicals used in the present study are of AR grade. M/s Sigma-Aldrich, and Merck, USA and M/s S.D. Fine Chem. Pvt. Ltd, Mumbai, India. Melting points were recorded on an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analyses were carried out using a Perkin-Elmer 240C CHN analyzer. ^{1}H-NMR spectra were obtained using 400 MHz and 100 MHz on a Bruker spectrometer (chemical shifts in δ ppm). Mass spectra were recorded using a micro spray Q-TOF MS ES Mass spectrometer.

General procedure for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones (3a) by Microwave method:

The $CuFe_2O_4$ nanoparticles (30 mg) was added to a solution of an 2-aminoacetophenone (10 mmol) and aromatic aldehyde (10 mmol) in 5 % methanolic NaOH (20 mL) and stirred for 05 minutes at room temperature. The whole mixture was transferred to a 100 ml round bottom flask and placed in CEM mars microwave and reaction mixture was irradiated for 30 minutes. Microwave power 400W and 120°C. The completion of the reaction was confirmed by TLC and it was allowed to cool to room temperature. After the reaction was complete, as indicated by TLC plates, the excess solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (hexanes–EtOAc, 20:1) to yield the desired product. The structures of all the synthesized molecules were established by spectral analyses (^{1}H NMR, ^{13}C NMR, and mass) data. All the synthesized compounds showed appropriate characteristic signals, which confirm their structures.

2-Phenyl-2,3-dihydroquinolin-4(1H)-one (3a)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, J = 8.0, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.36–7.30 (m, 4H), 6.78 (t, J = 7.2 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 4.70 (d, J = 8.0, 1H), 4.64 (s, 1H, NH), 2.80-2.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.4, 151.6, 141.2, 136.1, 128.8, 128.2, 127.5, 126.5, 119.2, 118.4, 115.6 (2C), 58.6, 46.4. HRMS (ESI): m/z calcd for $C_{15}H_{13}NONa$ (M+Na)$^+$: 246.1054; found: 246.1056.

2-(4-Methylphenyl)-2,3-dihydroquinolin-4(1H)-one (3b)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, J = 8.0, 1H), 7.36–7.28 (m, 3H), 7.20–7.10 (m, 2H), 6.78 (t, 1H), 6.68 (d, J = 8.0 Hz, 1H), 4.68 (m, 1H), 4.46 (s, 1H, NH), 2.90-2.80 (m, 2H), 2.35 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.8, 151.8, 138.4, 138.6, 136.5, 129.2, 128.4, 127.6(2C), 126.4, 119.8, 118.2, 116.2, 58.4, 46.2, 21.6. HRMS (ESI): m/z calcd for $C_{16}H_{15}NONa$ (M+Na)$^+$: 260.0868; found: 260.0870.

2-(4-Methoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (3c)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 8.0, 1H), 7.38–7.35 (m, 2H), 7.30–7.28 (m, 1H), 6.95–6.80 (m, 2H), 6.76–6.74 (m, 1H), 6.64 (d, J = 8.0 Hz, 1H), 4.68 (m, 1H), 4.46 (s, 1H, NH), 3.82 (s, 3H), 2.90–2.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 158.4, 151.2, 134.5, 133.6, 127.5, 126.7, 119.4, 118.6, 116.4, 114.6, 57.0, 55.6, 46.4. HRMS (ESI): m/z calcd for $C_{16}H_{15}NO_2Na$ (M+Na)$^+$: 276.1090; found: 276.1092.

2-(4-Chlorophenyl)-2,3-dihydroquinolin-4(1H)-one (3d)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, J = 8.0, 1H), 7.38–7.32 (m, 5H), 6.82 (t, 1H), 6.71 (d, J = 8.0, 1H), 4.68 (dd, J = 12.5, 1H), 4.56 (s, 1H, NH), 2.78 (s, 1H), 2.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.6, 151.4, 138.4, 136.2, 134.4, 129.6, 127.2, 127.4, 119.2, 118.4, 115.6, 56.9, 46.8. HRMS (ESI): m/z calcd for $C_{15}H_{12}ClNONa$ (M+Na)$^+$: 280.0852; found: 280.0852.

2-(4-Bromophenyl)-2,3-dihydroquinolin-4(1H)-one (3e)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.0, 1H), 7.54–7.46 (m, 2H), 7.38–7.32 (m, 3H), 6.80–6.78 (m, 1H), 6.72 (d, J = 8.0, 1H), 4.72 (dd, J = 11.4, 1H), 4.48 (s, 1 H, NH), 2.86–2.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.8, 151.6, 140.6, 135.3, 132.5, 128.8, 127.6, 122.6, 119.6, 118.2, 116.6, 58.4, 46.8. HRMS (ESI): m/z calcd for $C_{15}H_{12}BrNONa$ (M+Na)$^+$: 325.1063; found: 325.1065.

2-(4-Fluorophenyl)-2,3-dihydroquinolin-4(1H)-one (3f)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, J = 8.0, 1H), 7.46–7.38 (m, 2H), 7.30 (dd, J = 8.0, 1H), 7.06–7.02 (m, 2H), 6.78 (t, 1H), 6.72 (d, J = 8.0 Hz, 1H), 4.72 (dd, J = 11.4, 1H), 4.56 (s, 1H, NH), 2.82 (dd, J = 12.5, 1H), 2.74 (dd, J = 12.5, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.8, 163.2, 152.4, 136.8, 135.6, 128.6, 127.4, 119.2, 118.8, 116.2, 115.6, 57.8, 46.8. HRMS (ESI): m/z calcd for $C_{15}H_{12}FNONa$ (M+Na)$^+$: 264.0946; found: 264.0948.

2-(4-Nitrophenyl)-2,3-dihydroquinolin-4(1H)-one (3g)

Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.0,

2H), 7.88 (d, J = 8.0, 1H), 7.64 (d, J = 8.0, 2H), 7.38–6.84 (m, 3H), 6.78 (d, J = 8.0 Hz, 1H), 4.92–4.86 (m, 1H), 4.58 (s, 1H, NH), 2.84–2.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.4, 152.2, 148.6, 135.9, 127.8, 127.6, 124.5, 119.4, 116.2, 58.4, 45.4. HRMS (ESI): m/z calcd for $C_{15}H_{12}N_2O_2Na$ $(M+Na)^+$: 291.1060; found: 291.1062.

Antioxidant Activity

As a continuation of our previous work on the synthesis and antioxidant activity of biologically active heterocycles,[35] in this work we aimed to design and study the DPPH antioxidant activity of 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

Results and Discussion

Recently, the large number of papers on the synthesis of nitrogen heterocyclic compounds that have appeared in recent years attests to the huge contemporary interest owing to its biodiversity. This article reports the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones from 2-aminoacetophenone and aryl aldehydes using $CuFe_2O_4$ nano particles as a mild and efficient catalyst under microwave method (Scheme 1).

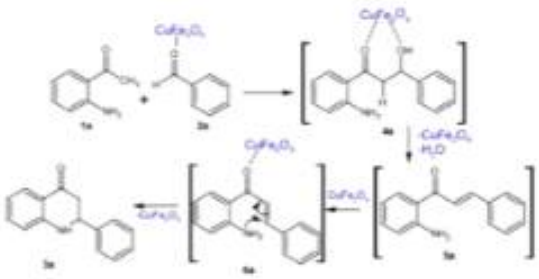


Scheme 1. Synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones: $CuFe_2O_4$ (30 mg); 5 % methanolic NaOH (20 mL); MW 30 minutes.

The proposed mechanism for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones is depicted in Scheme 2 based on our previous work.[35] In the initial step, reactants get adsorbed on the surface of the catalyst. The enhanced surface area and surface functional groups present on the $CuFe_2O_4$ surface facilitates better adsorption of reactant molecules. The synergistic effect of both Cu^{2+} and Fe^{3+} on the physical and chemical properties of $CuFe_2O_4$ contributed towards its catalytic activity.[35] The $CuFe_2O_4$ catalyst activates the carbonyl group of the aldehyde via co-ordination of vacant orbital present on $CuFe_2O_4$ with carbonyl oxygen to afford the intermediate 4a through the protonation of aldol adduct 5a with methanol, which undergoes intramolecular cyclization to yield final product 3a via 6a (Scheme 2).

Catalytic activity studies

As mentioned in Table 1, the maximum yield of 2-aryl-2,3-dihydroquinolin-4(1H)-ones was obtained using 30 mg of catalyst after 30 min in microwave method. A lower amount of catalyst dramatically decreased the reaction yield despite increasing the reaction time. To illustrate the importance of $CuFe_2O_4$ MNPs for these reactions. However, the selected $CuFe_2O_4$ as a highly efficient, reusability and operational simplicity and it is easily collected with an external magnet for reuse to prevent loss of the catalyst. To our delight, $CuFe_2O_4$ is the best heterogeneous nanocatalyst to afford different 2-aryl-2,3-dihydroquinolin-4(1H)-ones under mild reaction conditions in high-to-quantitative yields. We have also conducted the reactions by conventional method compare to the microwave method. The results indicate that, microwave method is the best method in terms of shorter reaction time and better yield.



Scheme 2. Proposed mechanism of $CuFe_2O_4$ catalysed synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones

Table 1. Optimization of catalyst loading and time for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

Entry	Catalyst	Catalyst loading (g)	Solvent	Traditional Method Time (hrs)	Yield (%)	M.W Method Time (min)	Yield (%)
1	$CuFe_2O_4$	0.002	MeOH	12	20	30	30
2	$CuFe_2O_4$	0.004	MeOH	12	30	30	42
3	$CuFe_2O_4$	0.008	MeOH	12	45	30	54
4	$CuFe_2O_4$	0.012	MeOH	12	60	30	70
5	$CuFe_2O_4$	0.016	MeOH	12	65	30	80
6	$CuFe_2O_4$	0.020	MeOH	12	80	30	95
7	$CuFe_2O_4$	0.030	MeOH	12	80	30	95

Solvent screening studies

The next parameter to be optimized was the type of solvent used for the synthesis. A series of solvents like MeOH, EtOH, CH_3CN, Toluene and DMF were used in the presence of $CuFe_2O_4$ MNPs and the results are given in Table 2. Optimization of solvent in the presence of enough catalyst showed that, Methanol was the better medium for the reaction at room temperature. Methanol was chosen as the solvent for further study because of its non-toxicity, low cost and wide availability as compared with organic solvents. Then, the amount of catalyst was optimized using Methanol as the solvent at room temperature in the model reaction.

Table 2. Optimization of solvent in the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

Entry	Catalyst	Catalyst loading (g)	Solvent	Traditional Method Time (hrs)	Yield (%)	M.W Method Time (min)	Yield (%)
1	$CuFe_2O_4$	0.030	EtOH	12	40	30	68
2	$CuFe_2O_4$	0.030	CH_3CN	12	30	30	55
3	$CuFe_2O_4$	0.030	Toluene	12	20	30	40
4	$CuFe_2O_4$	0.030	DMF	12	20	30	30
5	$CuFe_2O_4$	0.030	MeOH	12	80	30	95

Effect of substituents

After optimizing the reaction conditions, in order to study the electronic effect of substituted aryl aldehydes, we repeated the reaction with a variety of substituted aryl aldehydes. The results are summarized in Table 3. The yield of products depends on both electronic effect among reactants and the polarity of carbonyl group in aldehydes. Both electron withdrawing and electron donating groups on reactant showed moderate to good yield.

Table 3. Synthesis and antioxidant activity of 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

Products[a]	R	Yield (%)[b]	M.P. (°C)	DPPH Method Percentage of inhibition	IC_{50} value (µg /mL)
3a	H	90	142–144	58.56	4.82 ± 0.26
3b	4-CH_3	90	156–158	42.62	3.08 ± 0.14
3c	4-OCH_3	95	146–148	76.42	2.12 ± 0.34
3d	4-Cl	85	168–170	38.43	5.48 ± 0.32
3e	4-Br	85	166–168	36.52	5.84 ± 0.08
3f	4-F	85	136–138	32.48	6.08 ± 0.22
3g	4-NO_2	80	196–198	50.92	4.82 ± 0.16
			Ascorbic acid	72.86	1.98 ± 0.08

[a]All the products were characterized by elemental analysis,1H NMR, ^{13}C NMR and Mass spectral studies. [b]Yields of isolated products.

Reusability of $CuFe_2O_4$-MNPs

The recyclability of $CuFe_2O_4$-MNPs was investigated in the synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones by selecting the reaction between 2-aminoacetophenone (1a) with benzaldehyde (2a) as a model reaction. The reaction was repeated five times and after each cycle, the catalyst was magnetically separated, washed and dried for the next run. The catalyst is regenerated by magnetic recovery followed by washing with ethanol. It was found out that $CuFe_2O_4$ catalyst can be reused several times without considerable loss in catalytic activity. The percentage yield with number of cycles is given in Fig. 1. These results show that the catalyst is stable under the reaction conditions and no significant leaching occurs.

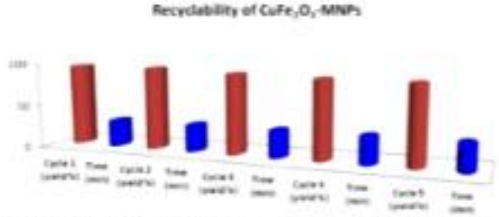


Figure 1. Recyclability of heterogeneous nano $CuFe_2O_4$ catalyst

In vitro antioxidant activity of 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

As explained in the introduction section, free radicals have aroused significant interest among scientists in the past decade. Their broad range of effects in biological system has drawn the attention of many experimental works. It has been proved that these mechanisms may be important in the pathogenesis of certain diseases and ageing. There are many reports that support the use of antioxidant supplementation in reducing the level of oxidative stress and in slowing or preventing the development of complications associated with diseases.

DPPH radical scavenging activity

DPPH, a stable free radical at room temperature, which produces a purple colour solution in methanol. It is reduced in the presence of synthesized 2-aryl-2,3-dihydroquinolin-4(1H)-ones, giving rise to uncoloured methanol solutions.[15] We found that they exhibited free radical scavenging activity against the stable free radical DPPH. Figure 2 and Table 3. All compounds 3a-3g expressed significant IC_{50} values for DPPH radicals. Compound 3c IC_{50} 2.12 ± 0.34 µg /ml. for DPPH radicals as shown in Table 3. The inhibitory activity gets higher depends on substitutions and presence of alkoxy group in 3c compared to other 2-aryl-2,3-dihydroquinolin-4(1H)-ones.

Structural activity relations observation demonstrates antioxidant activity depends on electronic factor of substituent aromatic benzene ring. Incorporation of electron releasing substituent at para-position improved activity compared to unsubstituted analogue. Introduction of electron withdrawing substituent at para-position lowers activity. Antioxidant activity of synthesized 2-aryl-2,3-dihydroquinolin-4(1H)-ones and IC_{50} values of synthesized compounds are presented in Table 3.

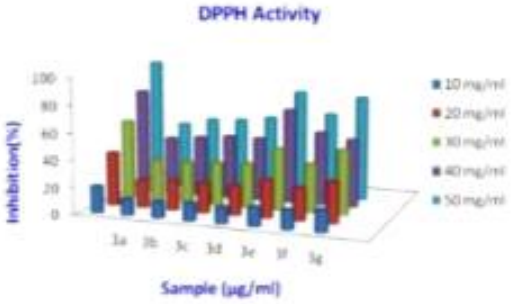


Figure 2. DPPH radical scavenging activity of 2-aryl-2,3-dihydroquinolin-4(1H)-ones (3a-g).

CONCLUSION

In summary, we have introduced $CuFe_2O_4$ heterogeneous magnetic nanocatalyst through a facile and simple microwave procedure. It was found that the $CuFe_2O_4$ nanocatalyst can be utilized for the one-pot synthesis of 2-aryl-2,3-dihydroquinolin-4(1H)-ones. This procedure includes further important aspects like the easy workup procedure, reusability of the catalyst, excellent yields, and environmentally benign reaction conditions. The synthesized compounds evaluated for their antioxidant activity. The alkoxy substituted 2-aryl-2,3-dihydroquinolin-4(1H)-ones showed significant antioxidant activity compare to other derivatives. Findings reveal that, the versatile scaffolds results in enhanced biological activity and provides scope for further research.

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CONFLICT OF INTEREST STATEMENT

Authors declare there is no conflict of interest for this work.

ETHICAL DECLARATIONS

No animals were used in this study.

REFERENCES AND NOTES

1. José Starvaggi, Roberta Ettari. Microwave-Assisted Organic Synthesis: An Eco-Friendly Method of Green Chemistry. *Pharmaceuticals (Basel)*, **2025**, 18(11), 1692.
2. Manoj B. Gawande, Sharad N. Shelke, Radek Zboril, Rajender S. Varma. Microwave-Assisted Chemistry: Synthetic Applications for Rapid Assembly of Nanomaterials and Organics. *Acc. Chem. Res.*, **2014**, 47(4), 1338–1348.
3. R. Veligeti, J. S. Anireddy, R. B. Madhu, A. Bendi, P. L. Praveen, D. S. Ramakrishna. Solvent-free synthesis of acridone based dihydropyrazine derivatives using $CuFe_2O_4$ nanoparticles as heterogeneous catalyst: molecular docking and in-vitro studies as anticancer agents. *J. Inorg. Organomet. Polym. Mater.*, **2023**, 33, 4039-4051.
4. A. K. Raigar, Manju, K. Saini, A. Guleria. $CuFe_2O_4$-catalyzed one-pot synthesis of α-substituted 2-benzofuranmethamines via tandem A3 coupling, 5-exo-dig cyclization, and 1,3-allylic rearrangement. *RSC Adv.*, **2025**,15, 32108-32116.
5. G. Satish, K. H. V. Reddy, K. Ramesh, B. S. P. A. Kumar, Y. V. D. Nageswar. An elegant protocol for the synthesis of N-substituted pyrroles through C–N cross coupling aromatization process using $CuFe_2O_4$ nanoparticles as catalyst under ligand-free conditions. *Tetrahedron Lett.* **2014**, 55 , 2596-2599.
6. A. R. Hajipour, M. Karimzadeh, G. Azizi. Highly efficient and magnetically separable nano-$CuFe_2O_4$ catalyzed S-arylation of thiourea by aryl/heteroaryl halides, *Chin. Chem. Lett.* **2014**, 25, 1382-1386.
7. G. Satish, K. H. V. Reddy, B. S. P. Anil, K. Ramesh, R. U. Kumar, Y. V. D. Nageswar. Direct C–H arylation of benzothiazoles by magnetically separable nano copper ferrite, a recyclable catalyst. *Tetrahedron Lett.* **2015**, 56, 4950-4953.
8. M. Ghobadi. Based on copper ferrite nanoparticles ($CuFe_2O_4$): catalysis in synthesis of heterocycles, *J. Synth. Chem.*, **2022**, 1, 84-96.
9. S. Sharma, P. Jakhar, H. Sharma. $CuFe_2O_4$ nanomaterials: current discoveries in synthesis, catalytic efficiency in coupling reactions, and their environmental applications, *J. Chin. Chem. Soc.*, **2023**, 70, 107-127.
10. D. Sanap, L. Avhad, S. Ahire, M. Mirzaei, D. Kumar, S. Ghotekar, N. D. Gaikwad. Insights into the promising heterogeneous catalysis of eco-friendly synthesized spinel $CuFe_2O_4$ nanoparticles for Biginelli reaction, *Res. Chem. Intermed.*, **2024**, 50, 3687-3711.
11. I. Akcok, A. Cagir. Synthesis of stilbene-fused 2′-hydroxychalcones and flavanones. *Bioorg. Chem*, **2010**, 38, 139-143.
12. M. Tomás-Navarro, F. Vallejo, F. A.Tomás-Barberán. Bioavailability and metabolism of citrus fruit beverage flavanones in Humans. In Polyphenols in Human Health and Disease; *Academic Press: Annapolis, MD, USA*, **2014**, 1, 537-551.
13. S. Kawais, K. Endo, T. Tokiwano, Y. Yoshizawa. Relationship between structure and antiproliferative activity of 1-azaflavanones, *Anticancer Res*, **2012**, 32, 2819–2826.
14. R. S. Varma, D. Kumar. Hypervalent iodine oxidation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones: An expedient route to naturally occurring 4-alkoxy-2-arylquinolines. *Tetrahedron Lett.* **1998**, 39, 9113–9116.
15. O. V. Singh, R. S. Kapil. A new route to 2-aryl-4-quinolones via thallium(III) p-tolylsulphonate–mediated oxidation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones. *Synth. Commun.* **1992**, 23, 277–283.
16. O. V. Singh, R. S. Kapil. Oxidation of 2-aryl-1,2,3,4-tetrahydro-4-quinolones: A novel entry for the synthesis of 2- and 3-arylquinoline alkaloids. *Synlett*, **1992**, 751–752.
17. R. N. Bhattacharya, P. Kundu, G. Maiti. Antimony Trichloride: An Efficient and Mild Catalyst for Cyclization of 2-Aminochalcones to the Corresponding 2-Aryl-2,3-Dihydroquinolin-4(1H)-ones, *Synth. Commun*, **2010**, 40, 476.
18. V. K. Rao, M. S. Rao, A. Kumar. Ytterbium (III) triflate: An efficient and simple catalyst for isomerization of 2-hydroxychalcone and 2-aminochalcones in ionic liquid, *J. Heterocycl. Chem*, **2011**, 48, 1356.
19. K. H. Kumar, D. Muralidharan, P. T. Perumal. Indium(III) Chloride/Silica Gel-Promoted Facile and Rapid Cyclization of 2-Aminochalcones to 2-Aryl-2,3-dihydroquinolin-4(1H)-ones under Solvent-Free Conditions, *Synthesis*, **2004**, 63-68.
20. J. I. Lee, H. J. Jung. An Efficient Synthesis of 2,3-Dihydro-2-phenyl-4-quinolones from 2-Aminoacetophenones, *J. Korean Chem. Soc.*, **2007**, 51, 106-110.
21. J. A. Donnelly, D. F. Farrel. The chemistry of 2-amino analogs of 2-hydroxychalcone and its derivatives, *J. Org. Chem*, **1990**, 55, 1757-1761.
22. R. Sakirolla, M. Yaeghoobi, N. A. Rahman. Synthesis of flavanones, azaflavanones, and thioflavanones catalyzed by PMA-SiO_2 as a mild, efficient, and reusable catalyst. *Monatsh Chem*, **2012**, 143, 797–800.
23. K. Hemanth Kumar, P.T. Perumal. A simple and facile solventless procedure for the cyclization of 2-amino- and 2-hydroxy-chalcones using silica-supported sodium hydrogen sulphate as heterogeneous catalyst, Can. J. Chem. 2006, 84, 1079.
24. B. Mondal, S. C. Pan. Primary amino acid catalyzed asymmetric intramolecular Mannich reaction for the synthesis of 2-aryl-2,3-dihydro-4-quinolones, *Org. Biomol. Chem*, **2014**, 12, 9789-9792.
25. M. Muthkrishnan, M. Mujahid, V. Punitharasu, D. A. Dnyaneshwar. Simple and Efficient Synthesis of 2-Aryl-2,3-Dihydroquinolin-4(1H)-ones Using Silica Chloride as a New Catalyst Under Solvent-Free Conditions, *Synth. Commun*, **2010**, 40, 1391-1398.
26. D. Kumar, G. Patel, B. G. Mishra, R. S. Varma. Eco-friendly polyethylene glycol promoted Michael addition reactions of α,β-unsaturated carbonyl compounds, *Tetrahedron Lett.* **2008**, 49, 6974-6976.
27. N. Ahmed, J. E. Van Lier. Alumina supported-$CeCl_3.7H_2O$–NaI: an efficient catalyst for the cyclization of 2-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1H)-ones under solvent free conditions, *Tetrahedron Lett.* **2007**, 48, 13-15.
28. X. Zheng, H. Jiang, J. Xie, Z. Yin, H. Zhang. Highly Efficient and Green Synthesis of Flavanones and Tetrahydroquinolones, *Synth. Commun*, **2013**, 43, 1023-1029.
29. A. L. Tőkés, L. Szilágyi. Resolution of (±)-2,3-Dihydro-2-phenyl-4(1H)-Quinolone. *Synth. Commun*, **1987**, 17, 1235-1245.
30. M. Cherghoum, M. Bahnous, A. Bouraiou, S. Bouacida, A. Belfaitah. An efficient and rapid intramolecular aza-Michael addition of 2-aminochalcones using ionic liquids as recyclable reaction media, *Tetrahedron Lett.* **2012**, 53, 4059-4061.
31. T. R. Ravikumar Naik. Therapeutic Significance of 1,4-Dihydropyridine Compounds as Potential Anticancer Agents, *Organic Synthesis-A Nascent Refook*, **2020**, 1, 217.
32. P. J. Bindu, T. R. Ravikumar Naik, S. Chandrashekar, K. M. Mahadevan. Synthesis, DNA binding, photocleavage, molecular docking stuies of 2-oxo-3-quinoline-3-oximes. *J. Mol. Chem*, **2022**, 2(2), 444.
33. P.J. Bindu, T.R. Ravikumar Naik, G. Krishnamurthy. Synthesis, DNA binding and molecular docking studies of 2H-benzo[b] [1,4] oxazines, *Biomed. Ther. Lett.*, **2025**, 12(1), 1153.
34. T. R. Ravikumar Naik, P. J. Bindu. Antimicrobial, antioxidant and molecular docking studies of Karanjin derivatives synthesized via Microwave assisted synthesis, *Biomed. Ther. Lett.*, **2026**, 13(1), 1852.
35. T. R. Ravikumar Naik, P. J. Bindu. Microwave assisted nano $CuFe2O4$ catalyzed synthesis of 2,5-Diarylthiazoles and evaluation of their antioxidant activity supported by molecular docking studies, *J. Mol. Chem*, **2026**, 6(1), 1702.