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Design, Antioxidant Activity and Molecular Docking Studies of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile

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Abstract: ***In the current study, we have developed the one-pot multicomponent green synthesis of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile, in a single molecular framework. The advances of this strategy include high product yields (90%), the development of cost-effectiveness, and a straightforward workup procedure that does not require any additional purification steps. The obtained structures of these newly synthesized compounds were confirmed by spectral analyses. The new compounds were tested for antioxidant and molecular docking studies. The free radical scavenging properties of compounds were examined by determining the capacity to scavenge superoxide anion formation (NADH), DPPH, hydrogen peroxide (H2O2) scavenging, and hydroxyl (.OH) scavenging activities. New compounds (4a-i) showed promising antioxidant activities having strong inhibitory activity. The molecular docking study against crystal structure of NADPH oxidase obtained supporting docking scores and showed notable binding interactions such as H-bond and hydrophobic.***

Keywords: 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile, Antioxidant, Free radical, DPPH, NADH, Molecular docking.

1. Introduction

The antioxidant activity plays an important role in the regulation of redox homeostasis and oxidative stress reduction [1,2]. 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 [1,2]. Thus, free radical scavenging has been suggested as potential therapeutic strategy for treatment of oxidative stress and inflammation-relative diseases.

In recent years, multicomponent reactions (MCRs) have emerged as a powerful approaches for the synthesis of bioactive compounds [3,4]. Multicomponent reactions (MCRs) are powerful tools for rapidly constructing compound libraries with sufficient molecular diversity and complexity [5-8]. MCRs can be used to generate multiple analogues of a hit molecule in a short time frame, thus lowering the costs of early medicinal chemistry efforts [5-8]. The design of MCR-based synthetic processes for approved drugs may also lead to overall lower production costs and has the potential to offer cost-effective medicines [5-8].

Sulfur-containing heterocyclic compounds are recognized as a crucial component of medicinal chemistry. In particular, fused thiochromenes are versatile sulfur-containing heterocyclic compounds that have received considerable interest in drug discovery because of their ability to act as crucial building blocks for synthesizing bioactive compounds [9,10]. In particular, these scaffolds have found utility in the design of anticancer, anti-HIV, antioxidant, and antimicrobial agents, among others. Despite their pharmacological potential, the synthesis of these scaffolds is less explored in contrast to their oxygen-containing counterparts [9,10].

Drug resistance in the modern era possess a challenge in tackling existing illnesses and emerging strands of new micro-organism leading to humanitarian crisis which necessitates the importance of renewed focus on scientific research to synthesize new classes of chemicals that will help in developing new medications. In particular, the sulfur-based heterocyclic derivatives like thiazole, thiopyran, benzothiopyran, thiophene, and thioazolidinone are frequently found as a part of several bioactive scaffolds [11,12]. Few mono/bi-cyclic scaffolds with a thio atom serve as building blocks for developing drugs and agricultural products [13-15]. As of 2018, over 285 sulfur-containing compounds were identified in the list of FDA-approved drugs for treating various ailments, and sulfonamides constitute the largest group in this series [13-15].

Green chemistry protects the environment, not by cleaning up, but by inventing new chemical processes that do not pollute the environment. Chemists from all over the world are using their creativity and innovation to develop new synthetic methods, reaction conditions, analytical tools, catalysts and processes under the new paradigm of Green Chemistry.16,17 Nanoparticles play a vital role in green chemistry, considering these heterogeneous $ZnFe_2O4$ magnetite nanoparticle (MNPs) catalysts can be simply separated from the reaction mixture by an external permanent magnet. Additionally, the catalyst can be easily recovered from the reaction mixture and reused, making the method more cost effective. Recently, $ZnFe_2O4$ magnetite

nanoparticle (MNPs) showed good catalytic behavior in organic transformations [16,17].

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 [18]. One of the computational chemistry approaches, known as molecular docking, have recently gained great popularity in the field of modern drug development [19]. 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 [19]. 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 [19].

The large number of papers on the synthesis of fused thiochromenes 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 $ZnFe_2O4$ MNPs catalyzed alternative synthetic strategy to achieve novel thiochromenes analogues. Taking inspiration from the above and as a part of our continuing research on the synthesis and biologically activity of fused heterocyles [20-24]. 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 three-component, one-pot synthesis of pharmacologically important 3-amino-1H-benzo[f]thiochromenes (Scheme 1) and studied their antioxidant and molecular docking studies.

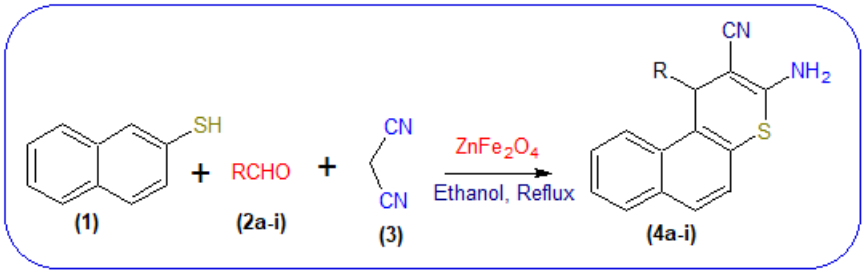
2. Result and Discussion

The large number of papers on the synthesis of fused thiochromenes 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.

2.1 Chemistry

As depicted in Scheme 1. Naphthalene-2-thiol (1) as a precursor for the synthesis of polyfused 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile. In a typical experimental procedure, naphthalene-2-thiol (1), aromatic aldehyde (2) and malononitrile (3) were stirred for 10 minutes at room temperature in the presence of a catalytic amount of $ZnFe_2O_4$ (30 mg) (**Scheme 1**). First we tried to carry out the reaction without adding any catalyst under neat condition, which could be expected to be the most economical method. Taking the reaction of benzaldehyde as an example, the mixture was stirred for about 12-14 hrs, a very poor yield was resulted (15%). For in-depth we evaluate the catalytic efficacy of some lewis bases in this reaction (**Table 1**). As is clear from the Table 1, $ZnFe_2O_4$ MNPs plays a crucial role in the success of the reaction in terms of the rate and the yields.

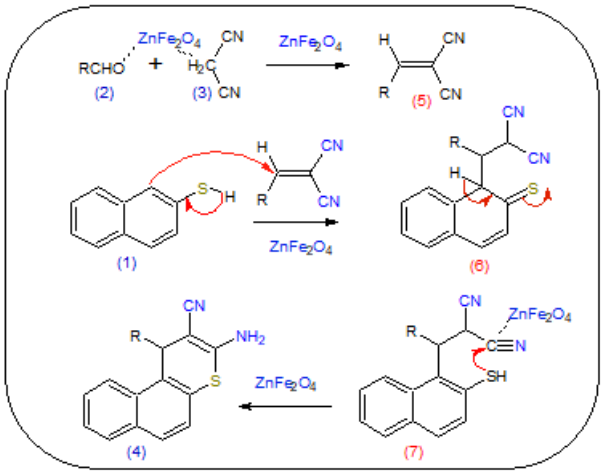


Scheme 1: Synthesis of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile.

As shown in Table 2, the three-component cyclocondensation reaction proceeded smoothly at 80-90 °C in ethanol to give the corresponding products (**4a-i**) in high yields. The electronic nature of the substituents on the aromatic ring shows a strong effect in terms of yields under these reaction conditions. The aromatic aldehydes containing electron-withdrawing groups (nitro group, halide) or electron-donating groups (alkyl group, alkoxy group) gave excellent to good yields of the corresponding 3-amino-1H-benzo[f]thiochromenes.

We proposed a possible mechanism (**Scheme 2**) to account for the reaction. First, the aromatic aldehyde (2) is condensed with malononitrile (3) to afford the α-cyanocinnamonitrile derivative (5). The step (2+3→5) can be regarded as a rapid Knoevenagel reaction of malononitrile and aromatic aldehydes can be carried out in acetonitrile without any catalyst, whereas in second step the reaction proceeds in presence of piperidine as a catalyst. The active methylene of (1) reacts with the electrophilic C=C double bond in (5) giving the intermediate (6), which tautomerizes into (7) latter is then cyclized by nucleophilic

attack of the SH group on the cyano (CN) moiety, results the (4) (**Scheme 1**).



Scheme 2: A plausible mechanism for the synthesis of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile.

The ^{1}HNMR spectrum of (**4e**) exhibited one singlet identified as amine (δ = 6.10 ppm) protons. Also, the aromatic protons are exhibited a characteristic multiplets at δ = 6.70-7.80 ppm).

Table 1: Effect of varying the catalysts

Sl. No	Catalyst	Time taken (hours)	Yield (%)
1	$ZnFe_2O_4$	2	82-90
2	K_2CO_3	6	45
3	K_2CO_3 + KI	5	54
4	Basic alumina	6	60
5	Sodium acetate	8	40
6	Na_2CO_3	6	45
7	None	12-14	15

The structure of (4e) was determined on the basis of its elemental analysis, ^{1}H NMR and mass spectral data. The mass spectrum of (4e) displayed molecular ion peak at m/z =328, which is consistent with 1:1:1 adduct of (1), (2e), and (3).

Table 2. Synthesis of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile.

Sl. No	R	Time taken (hours)	Yield (%)	M. P. (°C)[a,b]
4a	C_6H_4	2	90	192-195
4b	4-$CH_3C_6H_4$	2	87	228-231
4c	3-$NO_2C_6H_4$	2	80	237-239
4d	4-$NO_2C_6H_4$	2	80	245-248
4e	4-$CH_3OC_6H_4$	2	86	195-198
4f	4-ClC_6H_4	2	85	240-243
4g	3,4-$CH_3C_6H_4$	2	85	235-238
4h	4-FC_6H_4	2	90	208-211
4i	4-BrC_6H_4	2	82	252-254

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

2.2. Biological Activity

2.2.1. In vitro antioxidant activity of 3-amino-1H-benzo[f]thiochromenes.

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.

2.2.1.1.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**, summarizes the 50% inhibition (IC_{50}) value of 4e IC_{50} 0.012±0.002 µg /mL, 4e IC_{50} 0.012±0.002 µg /mL and 4h is IC_{50} 0.017±0.002 µg /mL. In the present study results on DPPH free radical scavenging activity shows that the compound 4a and 4b are greater scavenging activity than Ascorbic acid [25,26].

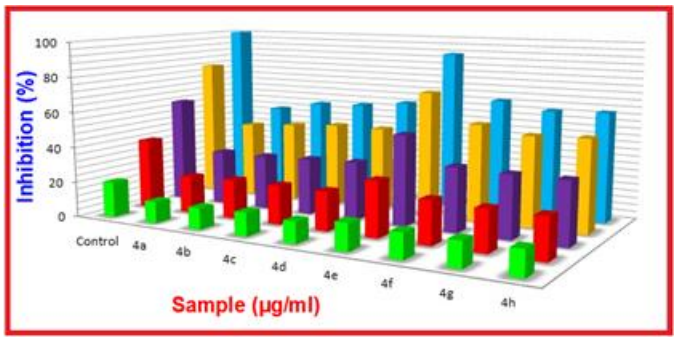


Figure 1: DPPH radical scavenging activity of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitriles (**4a-i**).

2.2.1.2.Hydrogen peroxide (H_2O_2) scavenging activity

H2O2 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 4a and 4b are higher than Ascorbic acid. H_2O_2 scavenging activities of 4a (IC_{50} 0.006 ± 0.004 mg/mL) and 4b (IC_{50} 0.008±0.002 mg /mL) were significantly ($p<0.05$) higher than Ascorbic acid (IC_{50} 0.060 ± 0.04 mg/mL) as shown in **Figure 2 and Table 3** [26].

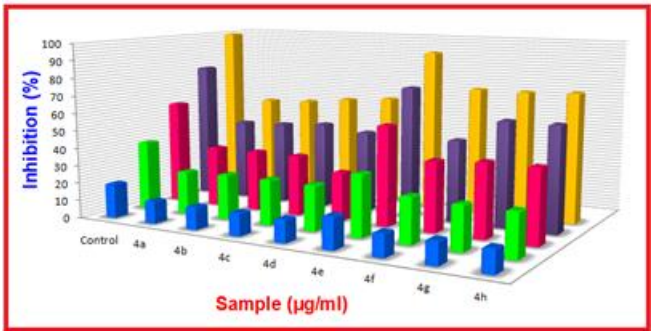


Figure 2: Hydrogen peroxide scavenging activity of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitriles (**4a-i**).

SAR studies showed that benzo[f]thiochromene nuclei at the position of 2 and 3 with specific hydrophilic groups increased activity compared to other hydrophobic groups. Additionally, choosing 4-nitrophenyl over 3-nitrophenyl substituted benzo[f]thiochromenes, 4-nitrophenyl substitution decreased antibacterial activity. Antioxidant activity of benzo[f]thiochromene is performed by DPPH and Hydrogen Peroxide radical scavenging methods taking Ascorbic acid as reference. Antioxidant activity is expressed as Percentage of inhibition. Compounds (4e, 4g and 4h in **Figure 2**) exerted enhanced activity in comparison to standard drug. Compounds (4d) displayed moderate potential. 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 (4a) recorded lowest IC50 value than standard drug Ascorbic acid and could be an efficient antioxidant [26].

Table 3: Antioxidant activity of Target Compounds (**4a-i**).

Entry	DPPH Method Percentage of inhibition	IC_{50} value ± standard error mean (µM)	Hydrogen peroxide method	IC50 value ± standard error mean (µM)
4a	38.26	-1.71± 0.12	35.92	-1.72± 0.12
4b	43.84	3.18 ± 0.34	41.45	3.37 ± 0.28
4c	56.15	4.09 ± 0.43	36.68	4.21 ± 0.15
4d	58.84	6.99 ± 0.11	55. 44	7.08 ± 0.18
4e	75.38	1.61 ± 0.34	71.20	1.82 ± 0.23
4f	65.07	3.72 ± 0.92	65.60	3.86 ± 0.16
4g	55.92	3.18 ± 0.70	45.80	3.57 ± 0.13
4h	71.92	1.65 ± 0.10	68.40	1.80± 0.18
4i	69.84	1.71 ± 0.21	64.12	1.76 ± 0.23
Ascorbic acid	80.76	1.51 ± 0.14	76.55	1.47 ± 0.39

Table 4: Binding affinities of synthesized compounds and interacting amino acids of NADPH oxidase (PDB ID: 2CDU).

Entry	Binding Energy (Kcal/mol)	H-bond
4a	−10.5	3H
4b	−10.3	–
4c	−8.6	2H
4d	−8.9	2H
4e	−9.4	3H
4f	−9.8	2H
4g	−9.7	3H
4h	−9.8	3H
4i	−10.1	3H
Ascorbic acid	−6.8	5H

2.2.1.3. 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.19 This method helps researchers prioritize the most promising candidates of drug discovery [19].

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).25 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 −8.6 to −10.5 Kcal/mol and ascorbic acid scored −6.8 Kcal/mol only. The molecular docking scores and binding interactions of compounds 4a-i are presented in **Figure 3 and Table 4**.

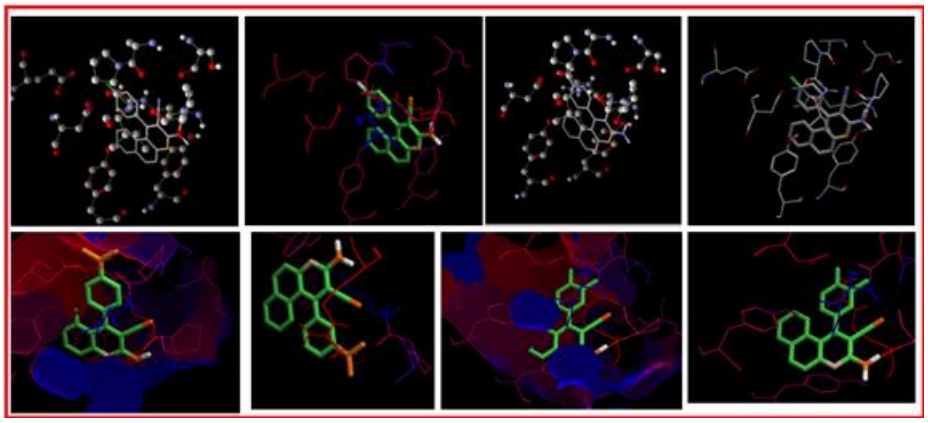


Figure 3: Molecular docking studies of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitriles (**4a-i)**.

SAR studies showed that 4-nitrophenyl over 3-nitrophenyl substituted benzo[f]thiochromenes docking scores are better compared to the other derivatives. Because nitro showed good binding activity with protein molecule.

The binding interactions of compounds at active sites amino acids of NADPH oxidase are matching to the interactions of ascorbic acid with many compounds. Except compounds 4c, remaining all compounds has demonstrated H-bond interactions which are critical for activity. For an example, the compound 4c scored good binding energy value of −8.6 Kcal/mol. It demonstrated H-bond interactions with amino acids among which π-π stacked and π-π T-shaped interactions with Tyr159 and Tyr188 of NADPH oxidase (Fig. 3). The standard compound ascorbic acid confirmed H-bond interactions with amino acids in cavity of NADPH oxidase (Fig. 4). The docking scores and binding interactions prove that these molecules could best fit into the pocket of NADPH oxidase.

3. Materials and Method

3.1 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 [26]. The activity is expressed as percentage of inhibition [26].

The antioxidant activity of benzo[f]thiochromene on DPPH radical scavenging activity was measured according to the literature method [26]. 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 1.

3.2 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.26 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**.

3.3 Molecular Docking Protocol

In present study, Autodock was used [19]. Autodock uses an empirical scoring function to calculate binding energy of protein-drug molecule [19]. The crystal structure of NADPH oxidase (PDB ID: 2CDU) [25] 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 [25].

4. Conclusion

In conclusion, we described the synthesis, design, antioxidant activity and molecular docking studies of 3-amino-1-phenyl-1H-benzo[f]thiochromene-2-carbonitrile.
All the compounds **4a-i** was screened for antioxidant activity by DPPH and hydrogen peroxide radical scavenging methods. The compound **(4a-i)** exhibited prominent IC_{50} value than standard drug ascorbic acid. Rest of the compounds exhibited moderate to good potency. Findings reveal conjugation of two versatile scaffolds results in enhanced biological activity and provides scope for further research. 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.

References

[1] 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.
[2] Erin. E. Battin, Julia. 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.
[3] T. R. Ravikumar Naik, S. A. Shivashankar. Heterogeneous bimetallic ZnFe2O4 nanopowder catalyzed synthesis of Hantzsch 1,4-dihydropyridines in water. Tetrahedron Letters, 2016, 57, 4046-4049.
[4] V.V. Throat, S. A. Dake, M.V. Katariya, R. P. Pawar, Cesium carbonate as a heterogeneous reusable and efficient catalyst for the synthesis of 2-amino-4H-chromene derivatives, Der Chemica Sinica, 2015, 6(6), 37-50.
[5] P. Gaikwad, S. Kamble, Microwave enhanced green and convenient synthesis of 2-amino-4H-chromenes in aqueous hydrotropic medium, Curr. Opin. Green Sustain. Chem, 2020, 3, 100014-100005.
[6] M.R. Naimi-Jamal, S. Mashkouri, A. Sharifi, An efficient, multicomponent approach for solvent-free synthesis of 2amino-4H-chromene scaffold, Mol. Divers, 2010, 14, 473477.
[7] M.M. Heravi, K. Bakhtiari, V. Zadsirjan, F. F. Bamoharram, O. M. Heravic, Aqua mediated synthesis of substituted 2amino-4H-chromenes catalyzed by green and reusable Preyssler heteropolyacid, Biol. Med. Chem. Lett., 2007, 17, 4262–4265.
[8] M. Saikia, L. Saikia, Sulfonic acid-functionalized MIL-101(Cr) as a highly efficient heterogeneous catalyst for one-pot synthesis of 2-amino-4H-chromenes in aqueous medium, RSC Adv., 2016, 6, 15846-15853.
[9] Manju, K. Saini, A. K. Raigar, A. Guleria, A Catalyst-Free One-Pot Multicomponent Green Strategy for the Synthesis of Spiroindene-1,3dione-Benzochromene/ Thio-Chromene Derivatives under Neat/Aqueous Conditions, 2023, 5859-5875.
[10] S. Murugappan, P.V. Kuthe, K.V.G.C. Sekhar, M. Sankaranarayanan, Recent developments in thiochromene chemistry, Org. Biomol. Chem., 2024, 22, 6045-6079.
[11] M. Feng, B. Tang, S.H. Liang, X. Jiang, Sulfur Containing Scaffolds in Drugs: Synthesis and Application in Medicinal Chemistry, Curr Top Med Chem, 2016,16(11),1200-16.
[12] M. Mustafa, J-Y. Winum, The importance of sulfur-containing motifs in drug design and discovery, Expert Opin Drug Discov, 2022, 17(5), 501-512.
[13] S. Pathania, R. K. Narang, R. K. Rawal, Role of sulphur-heterocycles in medicinal chemistry: An update, Eur J Med Chem, 2019, 180, 486-508.
[14] K. Laxmikeshav, P. Kumari, N. Shankaraiah, Expedition of sulfur-containing heterocyclic derivatives as cytotoxic agents in medicinal chemistry: A decade update, Med Res Rev, 2022, 42(1), 513-575.
[15] K.A. Scott, J.T. Njardarson, Analysis of US FDA-Approved Drugs Containing Sulfur Atoms, Top Curr Chem, 2018, 376(1),5.
[16] 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.
[17] A. Khazaei, A. Ranjbaran, F. Abbasi, M. Khazaei, A. R. Moosavi-Zare. Synthesis, characterization and application of ZnFe2O4 nanoparticles as a heterogeneous ditopic catalyst for the synthesis of pyrano[2,3-d] pyrimidines. RSC Adv., 2015, 5, 13643.
[18] J.D.S. Costa, R.D.S. Ramos, K.D.S.L. Csta, 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. Macêdo, 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.
[19] T. R. Ravikumar Naik, Therapeutic Significance of 1,4-Dihydropyridine Compounds as Potential Anticancer Agents, Organic Synthesis-A Nascent Relook. 2020, 1, 217.
[20] 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.
[21] 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.
[22] 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.
[23] 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.
[24] 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.
[25] 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.
[26] H. R. Prakash Naik, H. S. Bhojya Naik, T. R. Ravikumar Naik, H. Raja Naika, K. Gouthamchandra, R. Mahmood, B. M. K. Ahamed, Eur. J. Med. Chem. 2009, 44, 981-989.

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