

Synthesis and Molecular Docking Studies of 6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones and 6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones

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**Synthesis and Molecular Docking Studies of 6-{2-(N-H/phenyl/tolyl)
aminothiazol-4-yl} flavones and 6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl}
flavones**

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Abstract

In consideration of the flavones and docking studies, a new series of flavone derivatives have been synthesized in two steps reaction. The cyclo-condensation of compounds 6-chloroacetyl flavone with N-H/phenyl/tolyl thioureas was carried out via refluxing with ethanol to prepare (6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones (1-3). Treatment of 6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones with acetyl chloride for the acetylation reaction on the nitrogen atom of the NH₂ or NHR group in the thiazole ring gave 6-{2(N-H/aryl/tolyl-N-acyl) aminothiazol-4-yl} flavone compounds (4-6) with the 60-90% yields. All the synthesized compounds were docked with one anti-COVID-19 target (PDB: 6Y2E) The docking studies showed binding affinity of all the compounds. The pharmacokinetics studies were conducted

with the help of pk CSM software, to help the estimation of the absorption, distribution, metabolism, and excretion (ADME) properties.

Keywords: chromone, flavone, NMR Spectra, docking studies.

Introduction: Flavones are aryl substituted benzopyrans (chromones) with 15 carbons in skeleton. Considering the position of the aryl group on chromone, they are classified into three types: 2-Aryl benzopyrans (flavones), 3-Aryl benzopyrans (isoflavones), and 4-Aryl benzopyrans (neoflavonoids) [1-3]. Thiazole is an important moiety with manifold biological applications such as antibacterial, antipsychotic, anticancer, analgesic, antiallergic, anti-inflammatory, antimalarial, antihypertensive, antioxidant, and antifungal [4-17]. 6-chloroacetyl flavone [18] was synthesized by the cyclo condensation reaction of 2-hydroxyl acetophenone and benzaldehyde.

Methodology:

Synthesis 6-(2-aminothiazol-4-yl) flavone [1]:

5 mmol (1.4925 g) of 6-chloroacetyl flavone was dissolved in 25 mL of absolute alcohol and then 5 mmol (0.380 g) of thiourea was added to it. Then reaction content was refluxed on water bath for 2-2:30 hrs. Product formation was monitored by thin-layer chromatography. A crystalline solid isolated during the refluxing was cooled, filtered, and treated with ethyl alcohol. The aqueous solution of ammonia was added to the solid, and the content were left overnight. The final obtained residue was filtered, washed with water, dried, and recrystallized with ethyl alcohol [19].

Chemical Formula: C₁₈H₁₂O₂N₂S

Molecular Weight: 320.37; **Yield:** 90%; **State:** Solid (amorphous); **Colour:** Light brown;

M.P.: 110°C

Elemental Analysis: Found: C, 67.48; H, 3.78; N, 8.74; O, 9.99; S, 10.01

Calculated: C, 67.45; H, 3.79; N, 8.76; O, 9.99; S, 10.01

IR (KBr) cm^{-1} : 672, 685, 731, 763, 843, 870, 908, 962, 1012, 1030, 1045, 1078, 1129, 1223, 1252, 1312, 1381, 1412, 1464, 1493, 1565, 1603, 1640

^1H NMR (CDCl_3) δ : A singlet of 2H of NH_2 group (attached to the C-2 of thiazole ring) at 2.50 δ , a singlet for 3H of C3-H and C8-H of chromone ring and C5-H of thiazole ring at 7.06 δ , a doublet of 1H of C7-H of chromone ring at 7.82 δ , a doublet of 1H of C5-H of chromone at 8.09 δ , a multiplet of 5H of phenyl ring at 7.35 δ .

Synthesis of 6-{2-(N-phenyl) aminothiazol-4-yl} flavone [2]:

5 mmol (1.4925 g) of 6-chloroacetyl flavone were dissolved in 25 ml of absolute alcohol and then 5 mmol (0.7600 g) of phenylthiourea was added to it. Then reaction mixture refluxed over water bath for 2-2:30 h. Product formation was checked by thin layer chromatography. A crystalline solid was separated during the refluxing was cooled, filtered, and washed with ethyl alcohol. The aqueous solution of ammonia was added to the solid, and the content was left overnight. The obtained product was filtered, washed with water, dried, and crystallized with ethyl alcohol [19].

Chemical Formula: $\text{C}_{24}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$

Molecular Weight: 396.46; **Yield:** 85%; **State:** Solid (thread like crystals); **Colour:** Pale yellow; **M.P.:** 118°C

Elemental Analysis: Found: C, 72.71; H, 4.07; N, 7.07; O, 8.07; S, 8.09

Calculated: C, 72.68; H, 4.08; N, 7.06; O, 8.09; S, 9.00

IR (KBr) cm^{-1} : 671, 685, 752, 780, 765, 849, 904, 1126, 1223, 1374, 1458, 1565, 1594, 1636, 1706

¹H NMR (CDCl₃) δ: A singlet of 2H of NHR group (attached to the C-2 of thiazole ring) at 2.50 δ, a singlet of C3-H of chromone ring at 6.86 δ, a multiplet of 10 H of two phenyl ring (one phenyl is at C-2 position of chromone ring and another is attached to nitrogen atom of NH₂ gp between 7.29-7.97 δ, a doublet of C5-H of chromone ring at 8.10 δ, a singlet of C8-H of chromone and C5-H of thiazole ring at 7.28 δ, a double doublet of C7-H of chromone ring at 8.28 δ.

Synthesis of 6-{2-(N-tolyl) aminothiazol-4-yl} flavone [3]

5 mmol (1.4925 g) of 6-chloroacetyl flavone dissolved in 25 mL of absolute alcohol and then 5 mmol (0.8300 g) of tolyl thiourea added to it. Then reaction content was refluxed on water bath for 2-2:30 h. A crystalline solid separated out during the refluxing was cooled, filtered, and washed with ethyl alcohol. Product formation was monitored by thin-layer chromatography. The aqueous solution of ammonia was added to the solid and left overnight. The obtained residue was filtered, washed with water, dried, and recrystallized with ethyl alcohol [19].

Chemical Formula: C₂₅H₁₈N₂O₂S

Molecular Weight: 410.49 **Yield:** 90%; **State:** Solid (crystals); **Colour:** light yellow; **M.P.:** 120°C;

Elemental Analysis: Found: C, 73.15; H, 4.42; N, 6.82; O, 7.80; S, 7.81

Calculated: C, 73.19; H, 4.44; N, 6.79; O, 7.79; S, 7.79

IR (KBr) cm⁻¹: 671, 685, 752, 780, 765, 849, 904, 1126, 1223, 1374, 1458, 1565, 1594, 1636, 1706

¹H NMR (CDCl₃) δ: A singlet of 2H of NHR group (attached to the C-2 of thiazole ring) at 2.50 δ, a singlet of C3-H of chromone ring at 6.86 δ, a multiplet of 5 Ar-H of (phenyl ring at C-2 carbon) of chromone between 7.95-7.97 δ, a multiplet of 4H of phenyl ring (attached to N atom

of NH₂ gp) between 7.29-7.78 δ , a doublet of C5-H of chromone at 8.10 δ , a singlet of C8-H of chromone and C5-H of thiazole at 7.28 δ , a double doublet of C7-H of chromone ring at 8.28 δ .

Synthesis of 6-{2-(N-acyl) aminothiazol-4-yl} flavone [4]:

5 mmol (1.6000 g) of 6-(2-aminothiazol-4-yl) was dissolved in 5 mL of pyridine solvent and then 5 mmol (0.3925) of acetyl chloride was added to it. The prepared reaction content was kept at room temperature for 24 h and then poured in ice-cold water. The obtained solid was washed with water, dried and recrystallized with DMF [20].

Chemical Formula: C₂₀H₁₄N₂O₃S

Molecular Weight: 362.40; **Yield:** 80%; **State:** Solid (needles shaped); **Colour:** Yellow; **M.P.:** 102°C

Elemental Analysis: Found: C, 66.28; H, 3.89; N, 7.73; O, 13.24; S, 8.85

Calculated: C, 66.25; H, 3.87; N, 7.75; O, 13.25; S, 8.87

IR (KBr) cm⁻¹: 671, 686, 755, 767, 850, 904, 1009, 1028, 1041, 1078, 1127, 1224, 1258, 1374, 1447, 1463, 1494, 1525, 1564, 1604, 1641

¹H NMR (CDCl₃) δ : A singlet for CH₃ gp in NHCOCH₃ between 1-3 δ , a singlet of C3-H, C8-H of chromone ring and C5-H of thiazole ring at 7.08, a multiplet of 5H of phenyl gp (attached to C-2 of chromone ring) of flavone between 7.51-7.85, a doublet of C5-H of chromone ring at 8.10, a double doublet of C7-H of chromone ring between 8.06-8.18.

Synthesis of 6-{2-(N-phenyl-N-acyl) aminothiazol-4-yl} flavone [5]

5 mmol (1.9800 gm) of 6-{2-(N-phenyl) aminothiazol-4-yl} was dissolved in 5 mL of pyridine solvent and then 5 mmol (0.3925) of acetyl chloride was added to it. The reaction mixture was added to ice-cold water after being allowed to stand at room temperature for 24 h. The achieved solid was treated with water wash, dried and recrystallized with DMF [20].

Chemical Formula: C₂₆H₁₈N₂O₃S

Molecular Weight: 438.50 **Yield:** 80%; **State:** Solid (needles); **Colour:** Yellow; **M.P.:** 96°C-100°C

Elemental Analysis: Found: C, 71.22; H, 4.14; N, 6.39; O, 10.95; S, 7.3

Calculated: C, 71.20; H, 4.17; N, 6.41; O, 10.93; S, 7.21

IR (KBr) cm⁻¹ : 670, 686, 754, 766, 780, 849, 905, 924, 957, 1027, 1042, 1078, 1099, 1127, 1192, 1224, 1259, 1282, 1308, 1372, 1447, 1463, 1494, 1567, 1603, 1640

¹H NMR (CDCl₃) δ: A singlet for CH₃ group in NHCOCH₃ between 1-3 δ, a singlet of C3-H of chromone ring at 6.84, a singlet of C5-H of thiazole ring and C8-H of chromone ring at 7.29, a multiplet of 10H of two phenyl rings as one is attached to C-2 of chromone ring and another is attached to Nitrogen atom between 7.38-7.73, a doublet of C5-H of chromone ring between 8.24-8.26, a double doublet C7-H of chromone ring between 7.93-7.95.

Synthesis of 6-{2-(N-tolyl -N-acyl) aminothiazol-4-yl} flavone [6]:

5 mmol (2.0500 g) of 6-{2-(N-tolyl) aminothiazol-4-yl} was dissolved in 5 mL of pyridine solvent and then 5 mmol (0.3925) of acetyl chloride was added to it. The prepared reaction content was left at room temperature for 24 h and then poured in ice-cold water. The achieved solid was washed with water, dried and recrystallized with DMF [20].

Chemical Formula: C₂₇H₂₀N₂O₃S

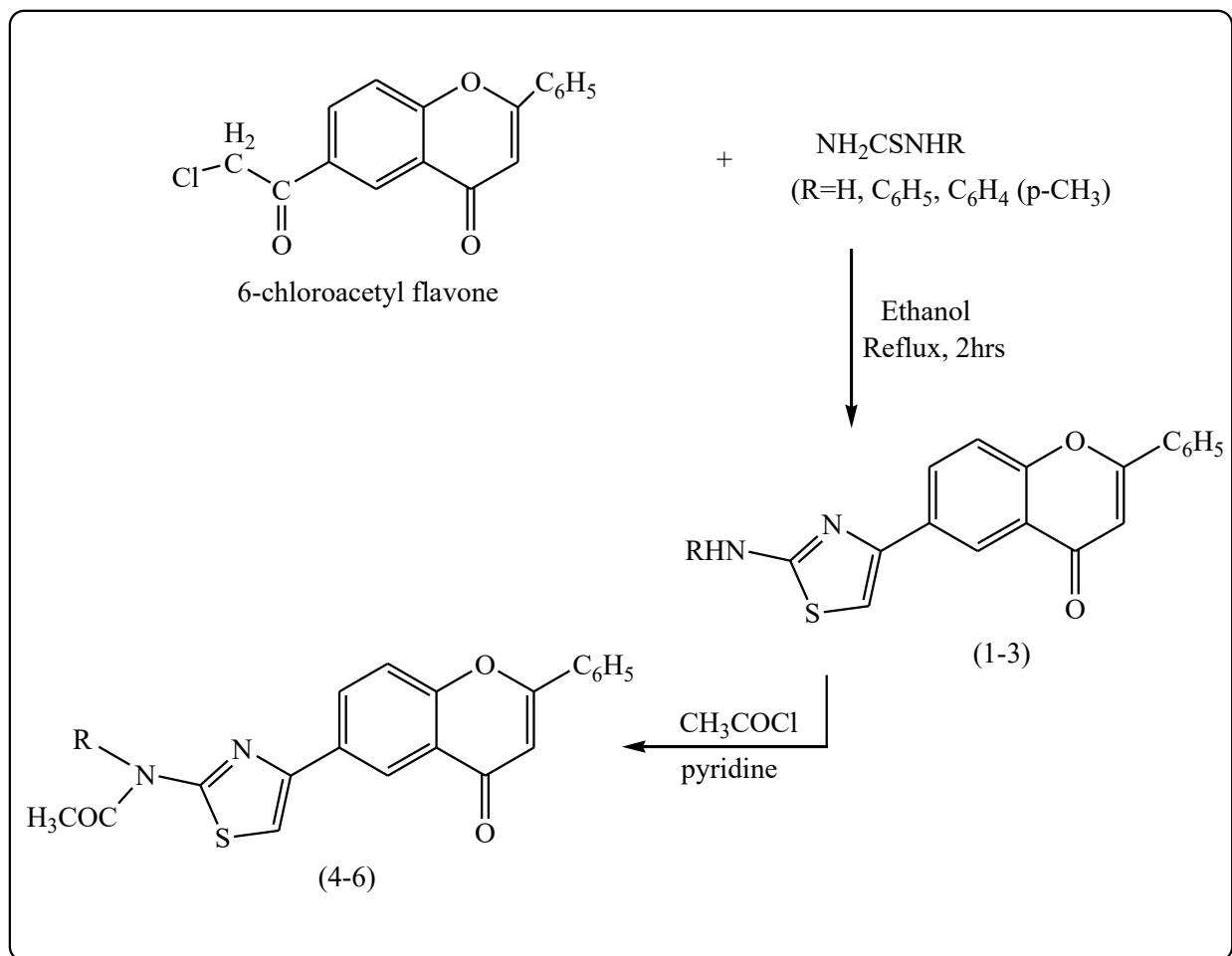
Molecular Weight: 452.52 **Yield:** 90%; **State:** Solid (needles); **Colour:** Brownish-yellow; **M.P.:** 90°C

Elemental Analysis: Found: C, 71.66; H, 4.45; N, 6.19; O, 10.61; S, 7.09

Calculated : C, 71.60; H, 4.48; N, 6.18; O, 10.64; S, 8.00

IR (KBr) cm^{-1} : 684, 753, 766, 780, 813, 848, 904, 924, 957, 1008, 1027, 1041, 1077, 1099, 1126, 1166, 1224, 1252, 1308, 1372, 1447, 1462, 1488, 1509, 1541, 1566, 1637, 1603

$^1\text{H-NMR}$ (CDCl_3) δ : A singlet for CH_3 group in NHCOCH_3 between 1-3 δ , a singlet of C3-H of chromone moiety at 6.84, a singlet of C5-H of thiazole ring and C8-H of chromone ring at 7.29, a multiplet of 10H of two phenyl rings as one is attached to C-2 of chromone ring and another is attached to N atom between 7.38-7.73, a doublet of C5-H of chromone ring between 8.24-8.26, a double doublet C7-H of chromone ring between 7.93-7.95



Scheme 1: Synthesis of 6-{2-(N-H/aryl/p-tolyl) aminothiazol-4-yl} flavones/chromones (1-3) & 6-{2-(N-H/phenyl/tolyl-N-acyl) aminothiazol-4-yl} flavones (4-6).

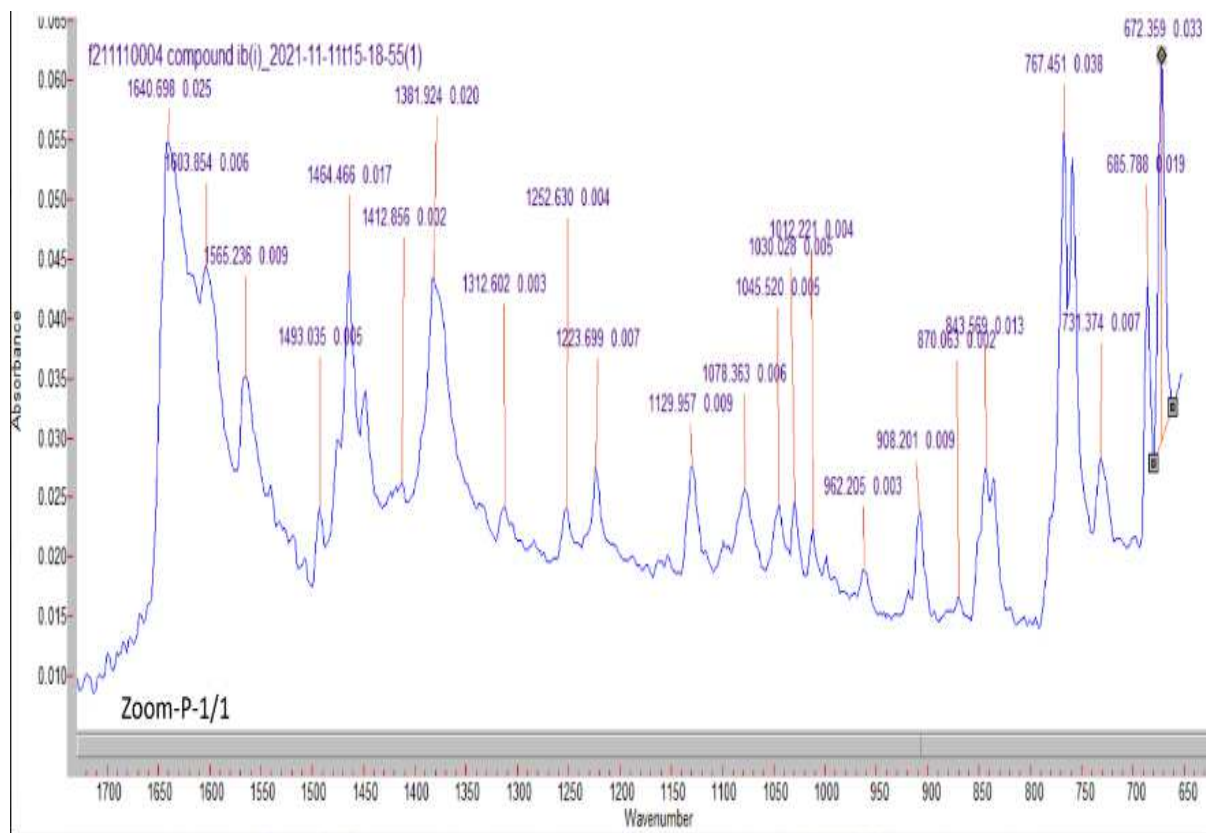


Figure 1: IR Spectra of 6-(2-aminothiazol-4-yl) flavone [1]

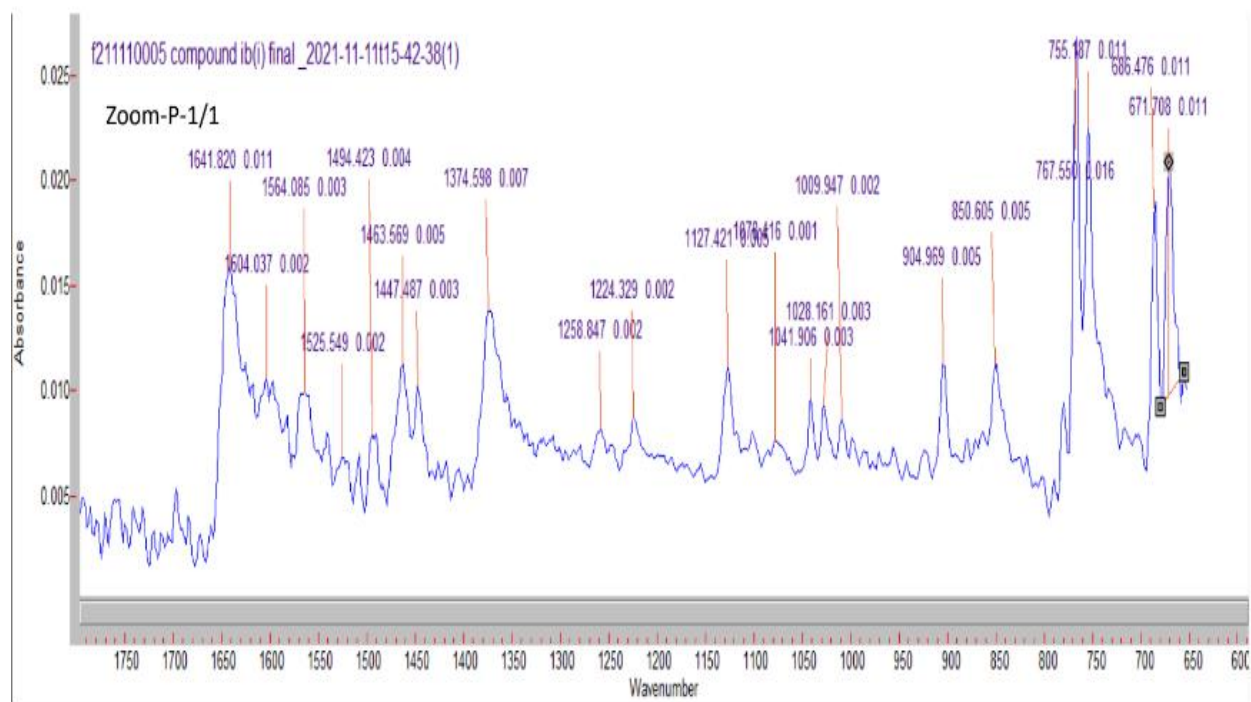


Figure 2: IR Spectra of 6-{2-(N-acyl) aminothiazol-4-yl} flavone [4]

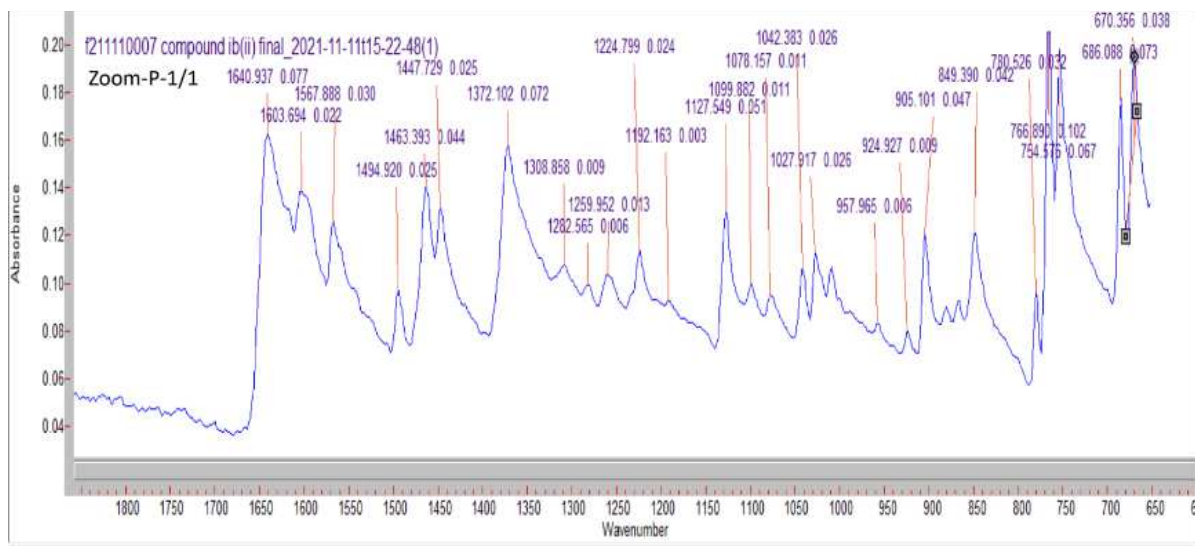


Figure 3: IR Spectra of 6-{2-(N-phenyl-N-acyl) aminothiazol-4-yl} flavone [5]

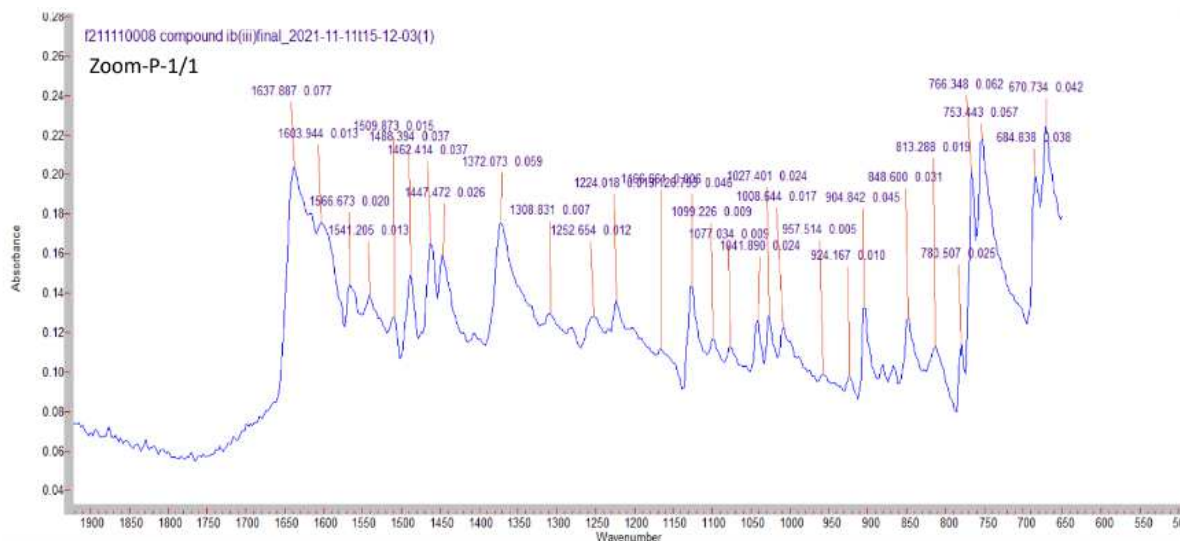


Figure 4: IR Spectra of 6-{2-(N-tolyl-N-acyl) aminothiazol-4-yl} flavone [6]

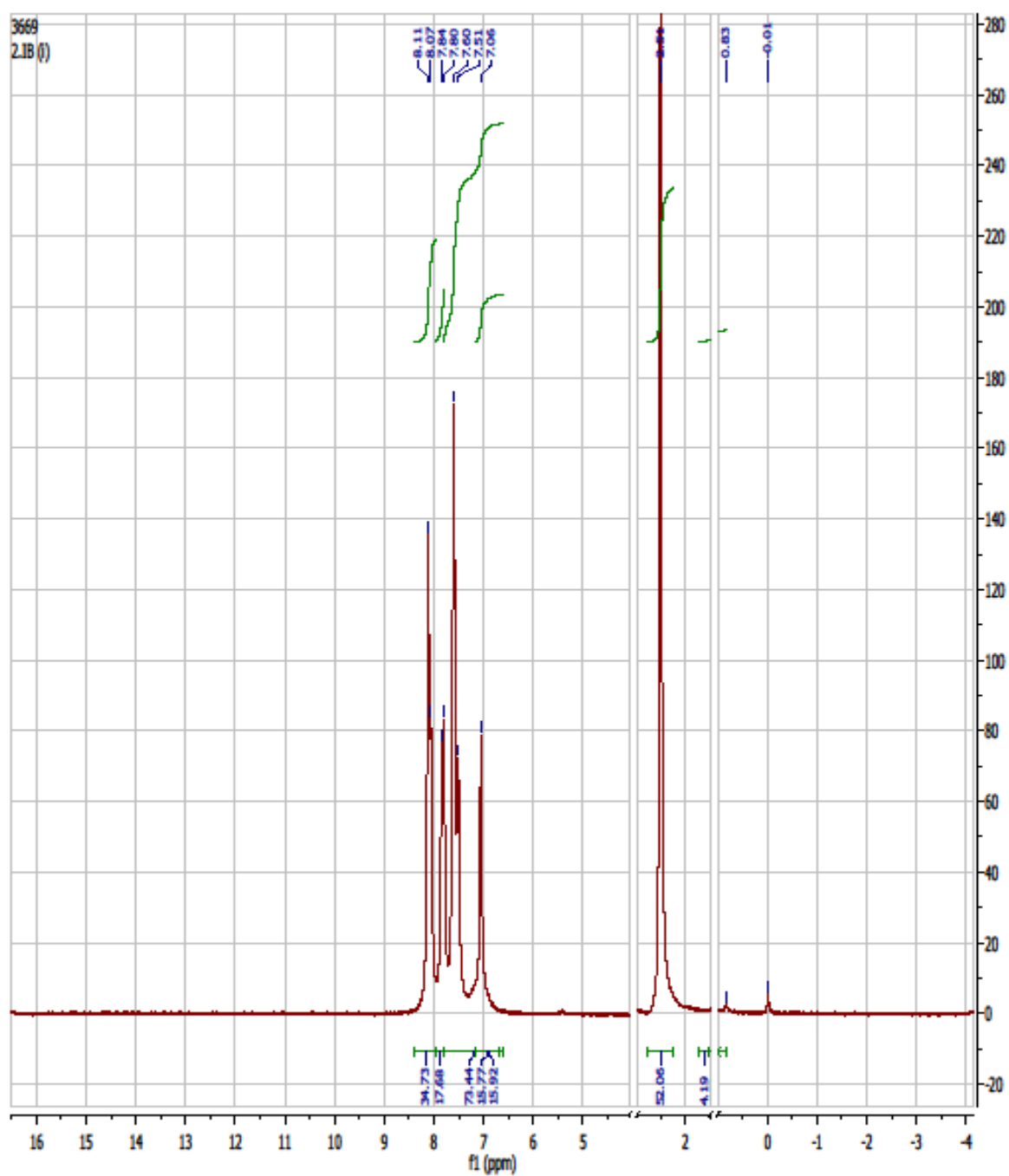


Figure 5: NMR spectra of 6-(2-aminothiazol-4-yl) flavone [1]

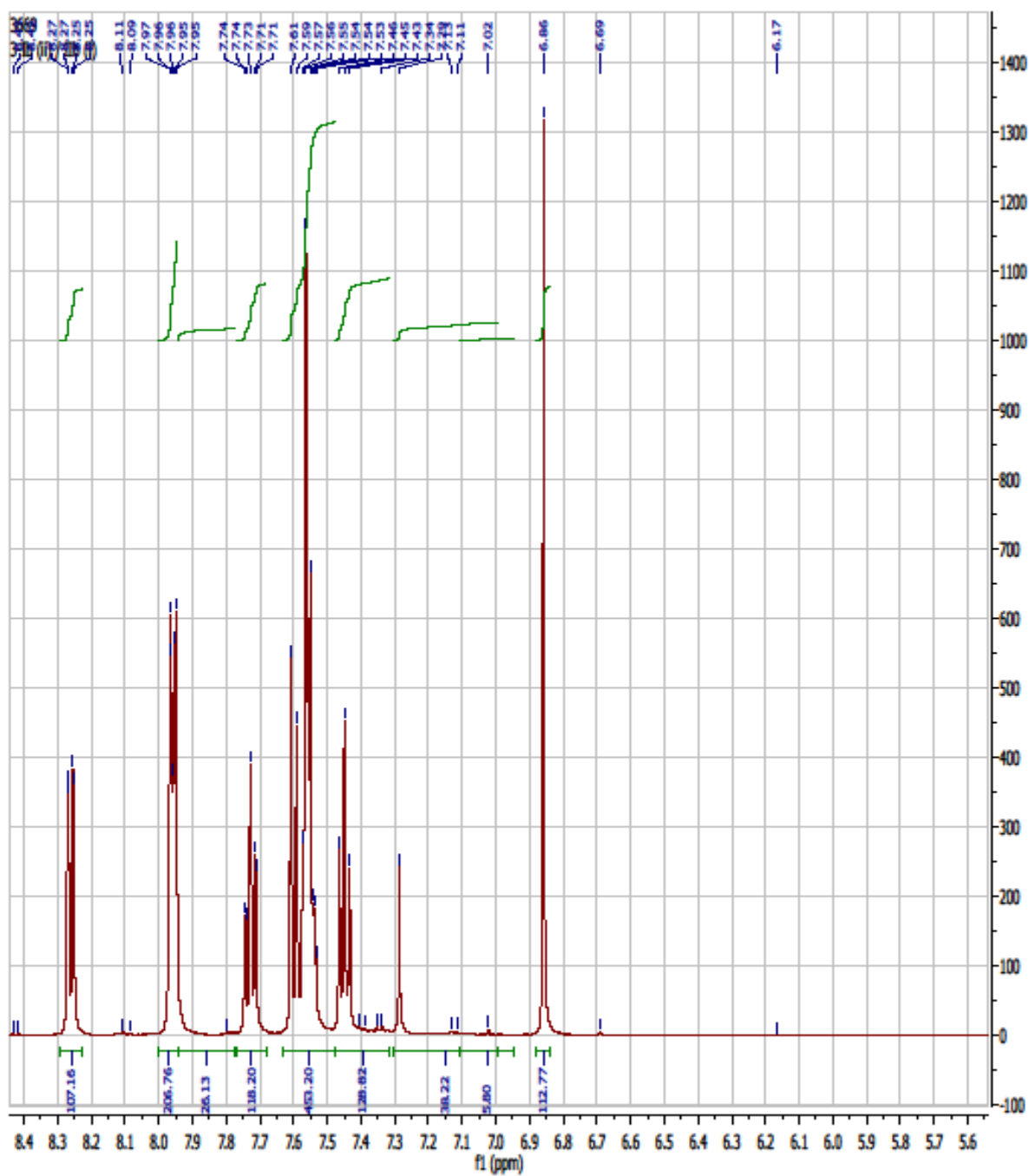


Figure 6: NMR spectra of 6-{2-(N-phenyl) aminothiazol-4-yl} flavone [2]

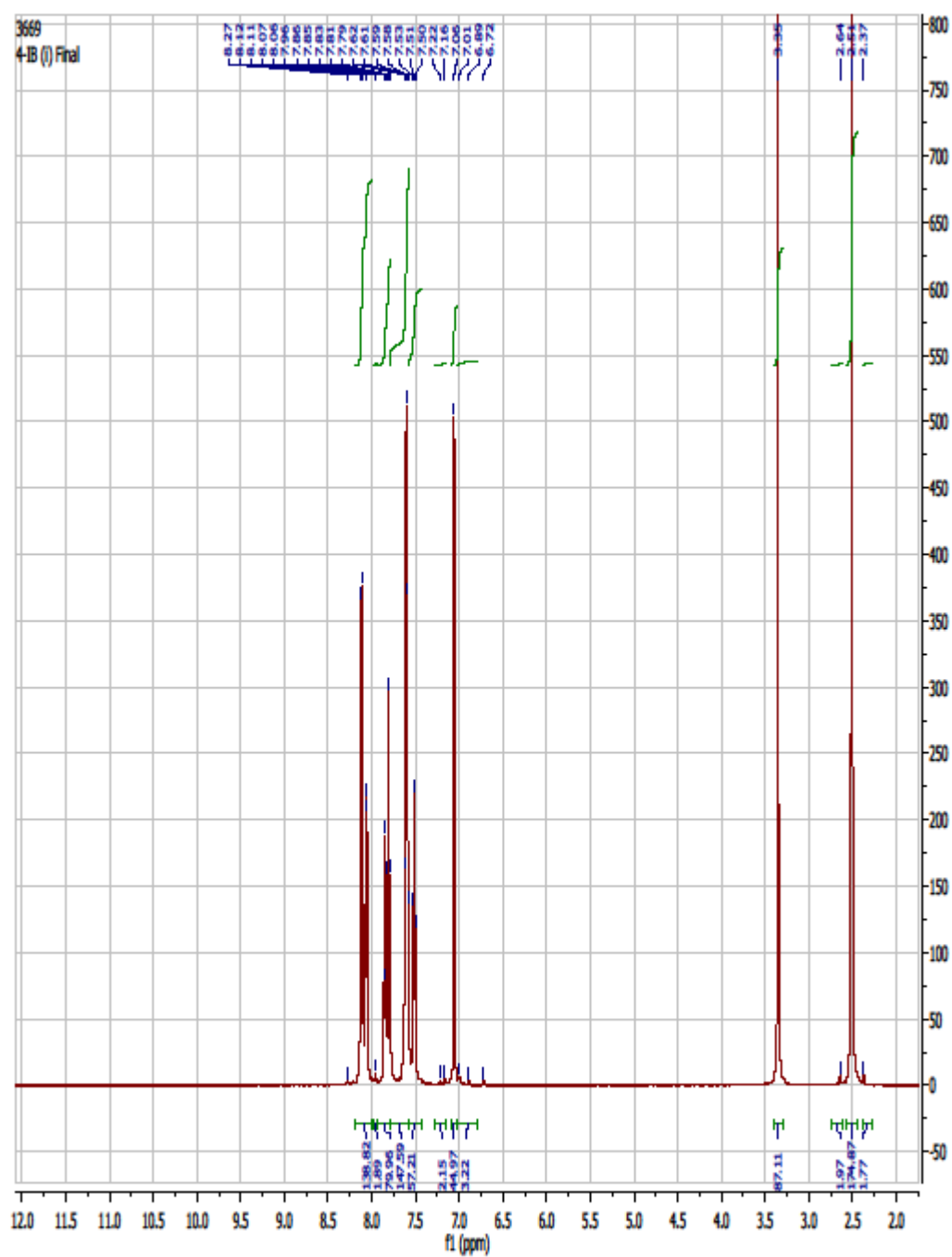


Figure 7: NMR spectra of 6-((N-acyl) aminothiazol-4-yl) flavone [4]

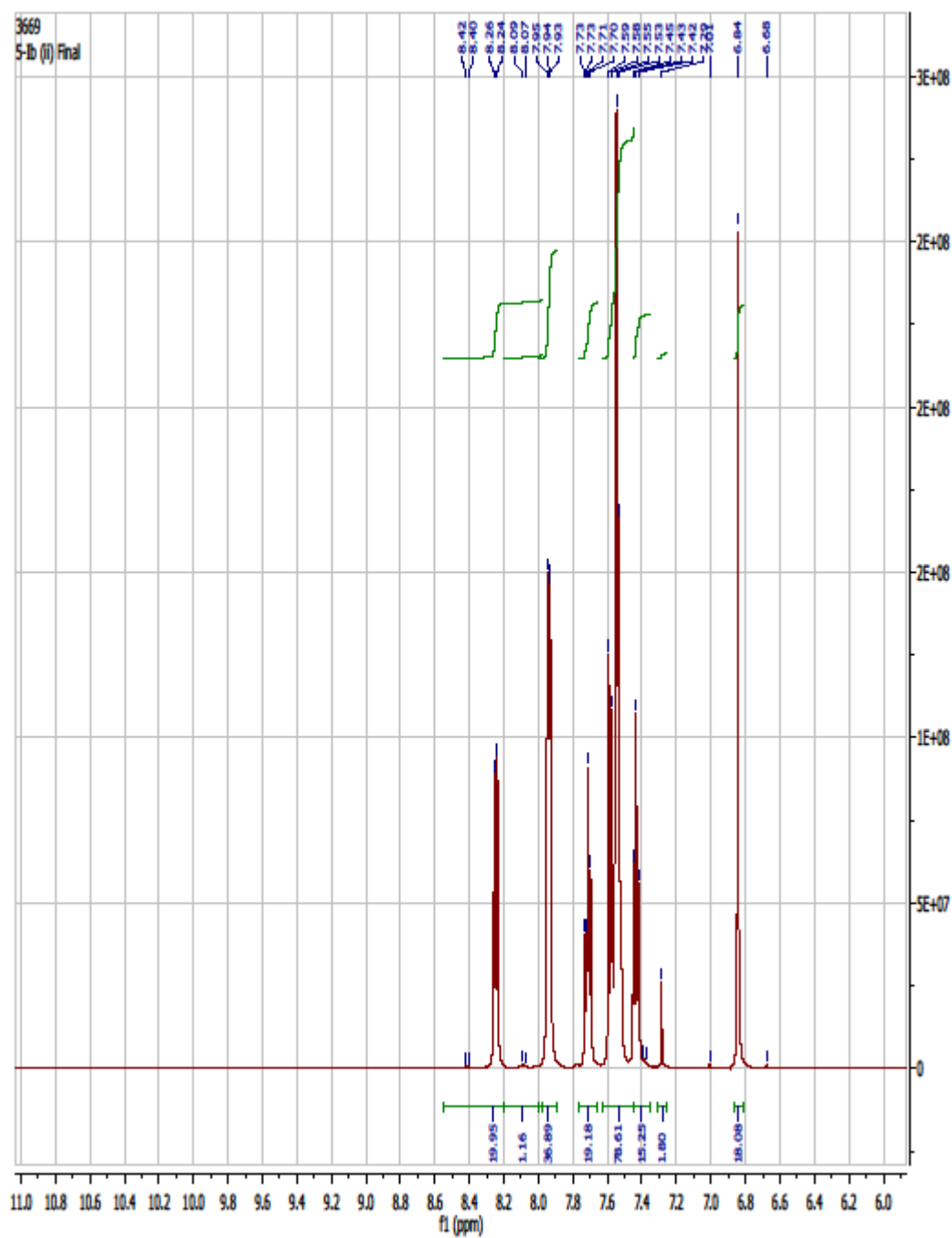


Figure 8: NMR spectra of 6-[(N-aryl-N-acyl) aminothiazol-4-yl] flavone [5]

Result and Discussion: The cyclo-condensation of compounds 6-chloroacetyl flavone with N-H/phenyl/tolyl thioureas was carried out via refluxing with ethanol to prepare compounds 1-3 (6-

{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones (Scheme-1). IR peaks at 1640 cm^{-1} and 1652 cm^{-1} , which were present in 6-chloroacetyl flavone because of the chloroacetyl side chain disappeared as this group was involved in a condensation reaction with the NH_2 group of thioureas to make 2(N-H/phenyl/tolyl) thiazole ring at C-6 of the flavone ring. One additional peak of N-H stretching for 1° amine and 2° amine appeared between 3350 cm^{-1} and 3000 cm^{-1} , along with the peak of C=O stretching for the chromone ring of flavone between 1640 cm^{-1} - 1706 cm^{-1} (Figure 1) for the compounds 1, 2, and 3 respectively. The ^1H NMR data of derivatives 1, 2, and 3 revealed that one peak of the singlet for 2H of the methylene group of the chloroacetyl side chain in 6-chloroacetyl flavone at $1.25\text{ }\delta$ disappeared in spectra as this group was involved in the formation of the thiazole ring. One additional peak of singlet for 2H of the $-\text{NH}_2$, and 1H of -NHR group of the thiazole ring appeared at $2.50\text{ }\delta$ - $2.00\text{ }\delta$ for the compounds 1, 2, and 3. Singlet for 1H of -NHR of the thiazole ring appeared at $2.50\text{ }\delta$ for the compounds 1, 2, and 3 (Figure 5 and 6). Treatment of 6-{2-(N-H/phenyl/tolyl) aminothiazol-4-yl} flavones (1-3) with acetyl chloride for the acetylation reaction on the nitrogen atom of the NH_2 or NHR group in the thiazole ring gave 6-{2(N-H/aryl/tolyl-N-acyl) aminothiazol-4-yl} flavone compounds (4-6) with the 60-90% yields (Scheme-1). One peak for the characteristic band for C=O str (pyran ring) was exhibited at 1641 cm^{-1} , 1641 cm^{-1} , and 1637 cm^{-1} for 4, 5, and 6 respectively (Figure 2-4). One more peak for the characteristic band C=O str ($-\text{NCOCH}_3$) was exhibited at 1604 cm^{-1} , 1604 cm^{-1} , and 1603 cm^{-1} for 4, 5, and 6 respectively respectively (Figure 2-4). One peak of singlet for 1H of $-\text{NHCOCH}_3$ group of the thiazole ring appeared at $2.50\text{ }\delta$ for the compound 4 (Figure 7) and disappeared in compound 5 and 6 due to the acetylation on N atom (Figure 8).

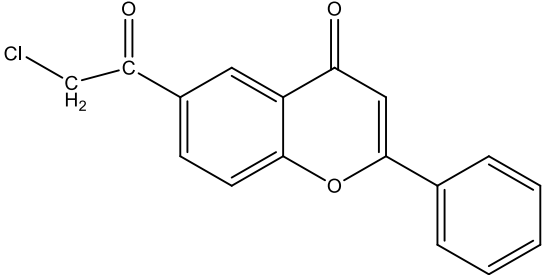
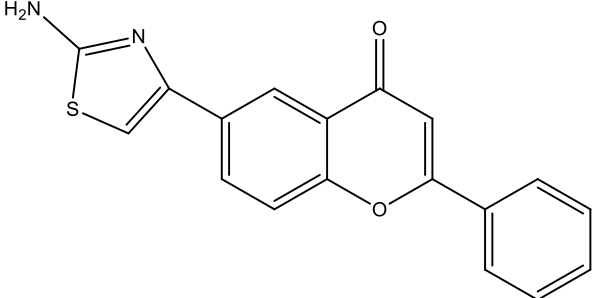
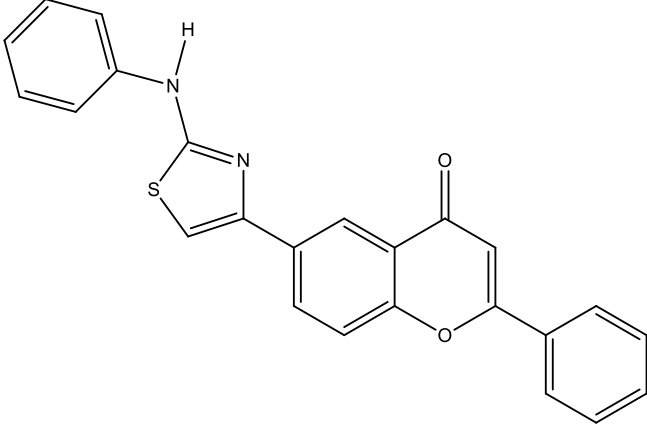
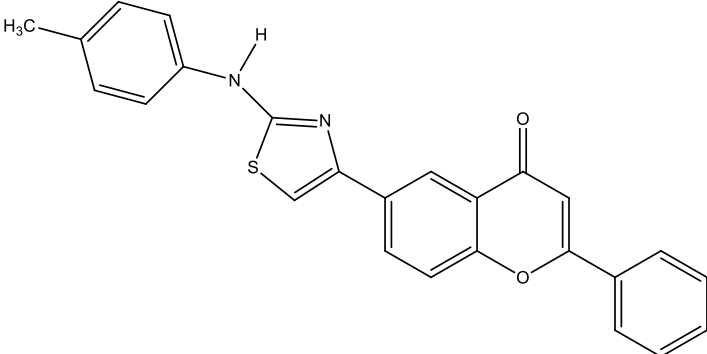
Molecular docking:

Evaluation of the physicochemical properties has helped in determining how well our drug candidate can potentially pass through cell membranes to reach its intended target receptor. The pharmacokinetics studies were conducted with the help of pkCSM software, which was able to help us estimate the absorption, distribution, metabolism, and excretion (ADME) based on the structure's molecular weight and lipid solubility index [21]. Physicochemical properties have been analysed with the help of Swiss ADME software. Docking studies were done with the help of molecular docking software known as Swiss Dock to find out whether drugs will have any potential for binding with their intended protein target or not. Table 1 consists of IUPAC names

and 2D structures of derivatives. Table 2 consists of the computed physicochemical properties of all compounds which depends on five parameters based on Lipinski's rule of five. These are the molecular rotational bonds ($n_{\text{Rot}} < 10$), weight ($\text{MW} < 500$ dalton), hydrogen bond acceptors ($\text{HBA} < 10$), topological surface area ($\text{TPSA} < 140$), hydrogen bond donors ($\text{HBD} < 5$), and number of violations < 4 . All seven compounds proceeded the RO5 rule and demonstrated zero violations (Table 2). Computed ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties have been reported in Tables 3 & 4. All compounds showed good ADMET data as they follow the standard value for all ADMET parameters, i.e., Caco-2 cell permeability ($\log P_{\text{app}}$ in 10^{-6} cm/s > 0.09), Intestinal absorption (human) % Absorbed (> 30), the volume of distribution (VD_{ss}) (human) {Numeric ($\log \text{L/kg}$)} (Low if < -0.15 and high. if > 0.45) [22]. All derivative showed excellent oral absorption, minimal toxicity, and no skin sensitivity. All derivatives have been found to be both non-toxic and non-irritating, so they have good oral bioavailability. Gastrointestinal absorption and the brain have been penetrated by using boiled-egg models (Figure 2) [23]. All derivatives come under the white region of the BOILED-EGG model except compound 6-chloroacetyl flavone. This derivative showed a high brain absorption level, whereas others showed good gastrointestinal absorption. Swiss Dock Server is a study platform for various medicine-related molecular docking tasks. This way, it generates the set of covalent bonds needed to properly attach both molecules for further analysis. Clean 2D and Clean 3D, prepared by Marvin Sketch Stool, have been used for this very purpose. When ready, ligands are exported in Mol2 files, while targets (selections) are saved in PDB (Protein Data Bank) format (PDB structure). All compounds have been studied and docked with one anti-COVID-19 target (PDB: 6Y2E). The docked images or binding poses of all the data are listed in Table 5, which was referenced in Figure 1. UCSF Chimera software has been used to assess molecular docking experiments based on hydrogen binding interactions, binding energy modes, full fitness score, Delta G, etc. With the help of UCSF chimera/other software, we docked all compounds, the new drug generation with their respective antiviral or anti-COVID-19 targets. Comparisons between docking results and the respective marketed drugs have been performed. It was found that all derivatives showed a good parameter range with the selected target when all derivatives were studied for docking with the anti-COVID-19 target. Compound 3 showed the best results as it binds to proteins with two hydrogen binding interactions, i.e., *LIG* 2.442 Å and *GLU* 2.026 Å with a full fitness score of -952.21 and Delta G of -7.08. When comparing these

derivatives to marketed drugs for the same purpose, they found a single hydrogen-binding interaction Umifenovir (*GLY* 2.190 Å) and Hydroxychloroquine (*ASN* 2.000 Å).

Table 1: Screened out compounds 4a, 8a (i-iii) and 10a (i-iii)

Compounds	2D structures of Compounds
6-chloroacetyl flavone	
6-(2-aminothiazol-4-yl) flavone [1]	
6-{2-(N-phenyl) aminothiazol-4-yl} flavone [2]	
6-{2-(N-tolyl) aminothiazol-4-yl} flavone [3]	

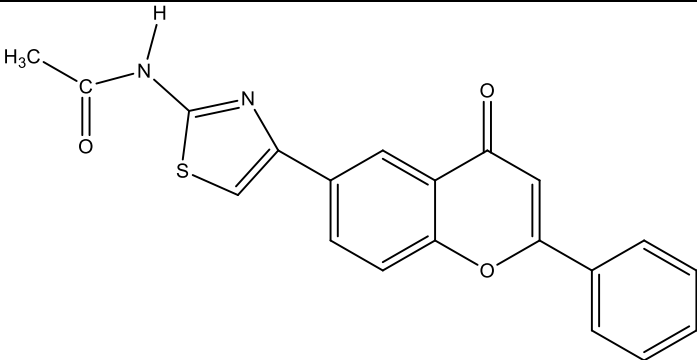
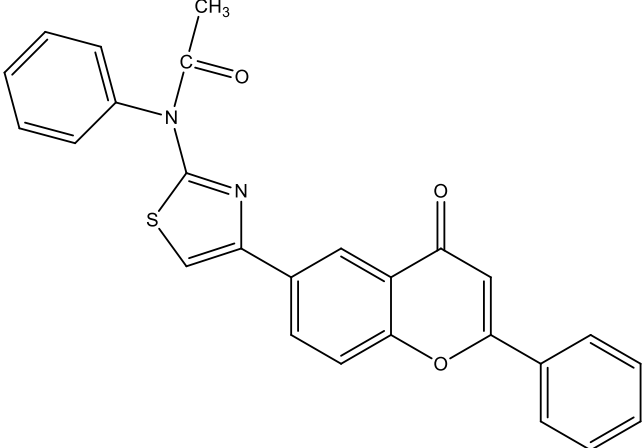
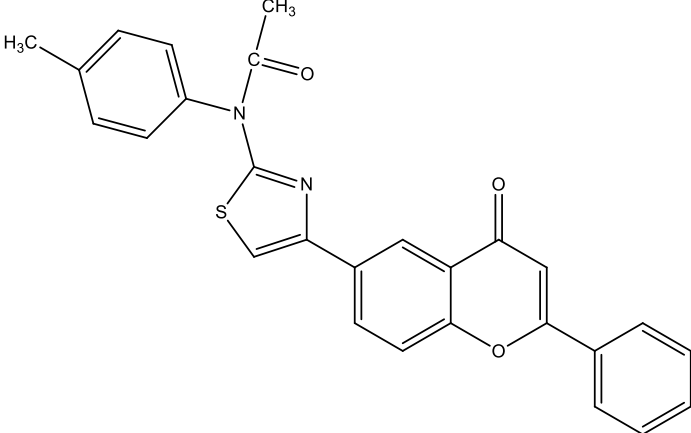
6-{2-(N-acyl) aminothiazol-4-yl} flavone [4]	
6-{2-(N-phenyl-N-acyl) aminothiazol-4-yl} flavone [5]	
6-{2-(N-tolyl -N-acyl) aminothiazol-4-yl} flavone [6]	

Table 2: Computed physicochemical properties of screened compounds 6-chloroacetyl flavone, 1,2,3,4,5, and 6.

Compounds	MW	nRot	HBA	HBD	TPSA	No. of violations
6-chloroacetyl flavone	298.72	3	3	0	47.28	0
1	320.37	2	3	1	97.43	0
2	396.46	4	3	1	83.37	0
3	410.49	4	3	1	83.37	0
4	362.40	4	4	1	100.44	0
5	438.50	5	4	0	91.65	0
6	452.52	5	4	0	91.65	0
Hydroxychloroquine	335.87	9	3	2	48.39	0
Umifenovir	477.41	8	4	1	80.00	0
Std. value	180-500	≤ 10	< 10	< 5	< 140	≤ 4

Table 3: Computed pharmacokinetic properties of screened compounds 6-chloroacetyl flavone, 1,2,3,4,5, and 6.

Compounds	Caco-2 permeability (log Pappin 10-6cm/s)	Intestinal absorption (human) (%Absorbed)	VDss (human) (logL/kg)	Fraction unbound (human)	Polyglyco-protein substrate (yes/No)
6-chloroacetyl flavone	1.341	97.466	0.23	0.203	No
1	0.944	93.815	0.213	0.325	No
2	1.076	90.93-	-0.003	0.335	No

3	1.065	91.159	0.044	0.35	No
4	0.947	93.305	0.289	0.292	No
5	1.09	94.735	-0.094	0.34	No
6	1.112	94.963	-0.055	0.352	No

Caco-2 cell permeability (log Papp in 10⁻⁶ cm/s > 0.09), Intestinal absorption (human) % Absorbed (> 30), VD_{SS} (human) {Numeric (log L/kg)} (Low if < - 0.15 and high. if > 0.45) [13].

Table 4: Computed pharmacokinetic properties of screened 6-chloroacetyl flavone, 1,2,3,4,5, and 6.

Compounds	Renal OCT2 substrate	AMES toxicity	hERG I inhibitor	Oral Rat Acute Toxicity (LD50)	Oral Rat Chronic Toxicity (LOAE)	Hepato-toxicity	Skin Sensitization
6-chloroacetyl flavone	No	Yes	No	2.082	1.835	No	No
1	No	Yes	No	2.435	0.597	Yes	No
2	No	Yes	No	1.785	-0.114	Yes	No
3	No	No	No	1.829	-0.067	Yes	No
4	No	No	No	2.38	0.67	Yes	No
5	No	No	No	2.222	-0/014	Yes	No
6	No	No	No	2.263	0.033	Yes	No

Table 5: Molecular docking results of screened compounds 6-chloroacetyl flavone, 1,2,3,4,5, and 6.

Anti-Covid19 Target: PDB: 6Y2E				
Compounds	Delta G	Full fitness	Energy (kcal/mol)	Hydrogen-Binding Interactions
6-chloroacetyl flavone	-6.13	-944.80	33.00	[1]. #0 ASN 72 HN-#1.75 LIG 1 O2 2.306 Å.
1	-6.11	-973.54	30.20	[1]. #1.158 LIG 1 H11-#0 LYS 137 O 2.201 Å.
2	-6.58	-952.05	51.13	[1]. #0 PHE 305 HN-#1.90 LIG 1 S1 2.499 Å.
3	-7.08	-952.21	51.33	[1]. #0 ASN 72 HN-#1.221 LIG 1 O2 2.442 Å. [2]. #1.221 LIG 1 H1-#0 GLU 14 O 2.026 Å.
4	-7.03	-986.31	27.16	[1]. #1.48 LIG 1 H1-#0 GLY 2 O 1.913 Å.
5	-6.98	-912.92	90.45	[1]. #0 PHE 305 HN-#1.65 LIG 1 S1 2.488 Å.
6	-6.79	-907.23	92.32	[1]. #0 ALA 7 HN-#1.216 LIG 1 O3 2.438 Å.
Hydroxychloroquine	-7.43	-1183.21	5.88	[1]. #1.16 LIG 1 H23-#0 ASN 119 O 2.000 Å.
Umifenovsir	-7.27	-1184.12	8.36	[1]. #0 GLY 71 HN-#01.49 LIG 1 O2 2.190 Å.

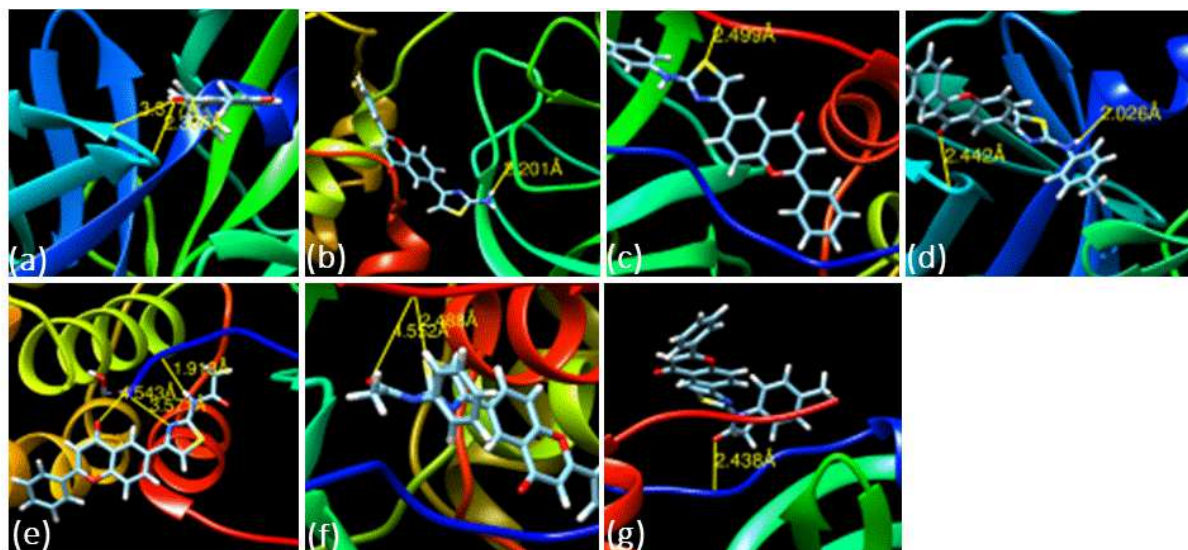


Figure 9: Molecular docking results of screened compounds 6-chloroacetyl flavone, 1,2,3,4,5, and 6 with Anti-Covid19 Target: PDB: 6Y2E.

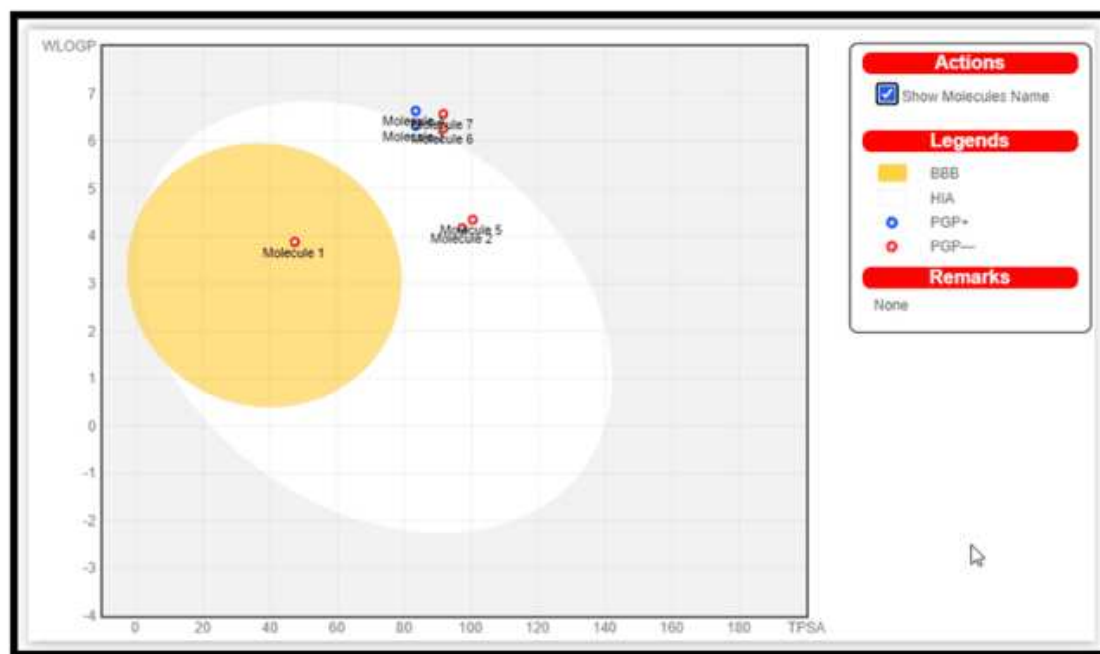


Figure 10: Boiled Egg Model of all seven compound

Conclusion: The study successfully established an efficient synthetic route for aminothiazole–flavone derivatives with good yields. Molecular docking against SARS-CoV-2 main protease (6Y2E) confirmed favorable binding interactions for all compounds, with Compound 3 showing comparatively superior affinity. Additionally, pharmacokinetic predictions supported their drug-likeness and potential oral bioavailability.

These findings provide a strong theoretical foundation for further in vitro and in vivo investigations toward the development of novel flavone-based antiviral agents.

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Ethics declarations

Ethics and consent to participate

Not applicable.

Consent to publish declaration

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing of interests

The authors declare no competing interests.

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