1. INTRODUCTION

Chalcones are important class of secondary metabolites which are precursors of many naturally-occurring plant pigments (Wong 1968). These small molecules are also used as starting materials in the synthesis of UV absorption filters in polymers, photorefractive polymers, photo sensitizers in color films, sweeteners in food technology and in holographic recording technology. They have significant commercial application in medical therapy due to the wide range of valuable biological activities which include antimutagenic, antibacterial, antiviral, anti-inflammatory, anti-ulcerative, hepatoprotective and anticancer activities (Forejtmikov *et al.* 2005).

![Chalcone Structure](image)

Chalcones are also be known as open chain flavanoids in which the two aromatic rings are joined by a three carbon, α, β unsaturated carbonyl system. Naturally occurring chalcones are all hydroxylated to a greater or lesser extent. The A ring substitution pattern is usually based upon the phloroglucinol (2, 4, 6-tri hydroxyl) since this part of the molecule is acetate derived. The B ring originates from a phenyl propanoid precursor and thus most commonly exhibits a 4- mono 3, 4, di or, 3, 4, 5 –trihydroxylation pattern. The numbering of the positions of substitution in the chalcone nucleus is reversed from that in most other flavanoids, i.e. the A ring is numbered 2′-6′and the B ring 2-6. Chalcone naturally derived from three acetate units and cinnamic acid.
Among flavonoids, this category of flavonoid precursor has been identified as interesting compounds that is associated with several biological activities.

The most common chalcones found in foods are phloretin and its glucoside phloridzin (phloretin 2′-0-glucose), chalonaringenin and arbutin. Phloretin and phloridzin are characteristic of apples. Chalonaringenin is characteristic of tomatoes and arbutin is characteristic of pears (Harborne et al. 1994). Table-1 shows the classification of chalcones from natural sources.

Table-1: Classification of natural chalcones.

<table>
<thead>
<tr>
<th>Class</th>
<th>Name of chalcones</th>
<th>Source</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-Hydroxychalcone</td>
<td>Isoliquiritigenin</td>
<td>Glycyrrhizaglabra</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>Carthamone</td>
<td>Carthamone</td>
<td>Carthamus tinctorius</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>3,4-Dihydroxychalcone</td>
<td>Butein</td>
<td>Rhus verniciflua</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>3,4,5-trihydroxychalcone</td>
<td>Robtein</td>
<td>Robinia pseudacacia</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>Chalcones lacking B-ring hydroxyls</td>
<td>Pedicin</td>
<td>Didymocarpus pedicellata</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>Retrochalcones( in this type ring hydroxylation patterns is reversed)</td>
<td>2,4-dihydroxy-4′,6-dimethoxychalcone</td>
<td>Imperata cylindrica</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td></td>
<td>Praecansone-A</td>
<td>Tephrosia pumila</td>
<td><img src="image" alt="Structure" /></td>
</tr>
</tbody>
</table>
2. REVIEW ON SYNTHESIS OF CHALCONE

Chalcones can be prepared by Claisen-Schimdt condensation between a benzaldehyde and an acetophenone in the presence of sodium hydroxide as a catalyst (scheme-1). This reaction has been found to work without any solvent at all - a solid-state reaction.

![Scheme-1](image1.png)

The chalcone derivatives having hydroxyl groups are prepared through base-catalyzed Claisen-Schimdt condensation of MOM-protected benzaldehydes with para-substituted acetophenones followed by acid catalyzed hydrolysis. In the reactions, the MOM-protected benzaldehydes are used instead of non-protected dihydroxylated ones, because the procedure with the free dihydroxylated benzaldehydes required long reaction time (more than one day) and relatively high temperature (above 60°C) which resulted in poor yields with unknown degraded products (Kim et al. 2008). Solid phase synthesis of Hydroxy chalcone derivatives has also be carried out (Cheng et al. 2000) (Scheme-2).

![Scheme-2](image2.png)
A series of chalcone derivatives were prepared via the reaction of cis–bicycle[3.2.0]hept-2-en-6-one with the respective arylaldehydes (Scheme-3) (Ceylan and Findik 2009)

\[
\text{cis-bicycle[3.2.0]hept-2-en-6-one} + \text{arylaldehyde} \rightarrow \text{chalcone}
\]

\[\text{R} = \text{mono substituted phenyl / thienyl/ furyl/ pyrrol ring}\]

Mandge et al. (2007) had synthesized 4-Dimethyl aminochalcone, 2-hydroxy dimethylaminochalcone and 2-hydroxy chalcones by a single step method. Wang (2009) shows the synthesis of chalcones by Claisen Schmidt condensation of substituted acetophenones with various aromatic aldehydes in the presence of iodine by grinding under solvent free conditions while Retab et al. (2009) synthesizes different chalcone analogue by grinding aryl aldehyde and acetophenone with anhydrous barium hydroxide (C-200) and methyl ketone and aromatic aldehyde respectively by grinding at room temperature in the absence of any solvent. Preparation of chalcones in the presence of different types of catalysts like phosphonium ionic liquid (Sarda et al. 2009), acyclic SO$_3$H functionalized ionic liquids (Fang et al. 2008), NKC-9 acidic resin (Jiang et al. 2008), SOC I$_2$/ethanol (Ivanova et al. 2008), potassium phosphate (Pore et al. 2007) had been reported for the efficient synthesis of chalcones. Xing (2009) describes palladium acetate-catalyzed synthesis of chalcones in water in the presence of 1-butyl-3-methylimidazolium hexafluorophosphate[bmim][PF$_6$]. Synthesis of chalcones with aromatic and heteroaromatic aldehyde in the presence of base (on the basis of Pyridine -2(1H)-one) (Kalashnikov et al. 2008) have been also reported. Six new chalcones were synthesized (Scheme-4) by condensing 2-acetyl pyridine with aldehyde derivative in diluted ethanolic potassium hydroxide solution (Prashad et al. 2008).
A series of 2-chloroquinolinyl chalcones (Scheme-5) and other chalcone derivatives were prepared by condensing aromatic aldehydes and methyl ketones to form the expected compounds, using solid sodium hydroxide as a catalyst in methanol at room temperature (Herencia et al. 1998).

\[
\text{R}_1\text{CH}_3 + \text{OHC-R} \xrightarrow{\text{NaOH}\;\text{CH}_3\text{OH}} \text{R-Substituted 2-chloroquinone}
\]

\[
\text{R}_1=\text{substituted phenyl/hetryl ring}
\]

Liu (2007) synthesized nine chalcones by using solid alumina-supported potassium fluoride (KF-Al2O3) as catalyst, in good yields by an aldol condensation of 4-nitroacetophenone with aromatic aldehyde under solvent-free and under microwave irradiation conditions. The microwave assisted synthesis of six chalcones was carried out by condensing the piperonal with acetophenones in presence of zinc chloride under solvent-free conditions (Saini et al. 2007). A series of \(\alpha,\beta\)-unsaturated ketones was synthesized by aldol condensation reaction of 2-acetyl-6-methoxynaphthalene and substituted benzaldehyde under solvent-free conditions using silica-sulfuric acid as acidic catalyst (Thirunarayanan 2007) (Scheme-6).

\[
\text{H}_3\text{CO-} + \xrightarrow{\text{SiO}_2\text{-H}_2\text{SO}_4\;\text{Solvent free 800C}} \text{Where X=H, m-NH}_2, \text{p-NH}_2, \text{m-Br, m-Cl, p-N(CH}_3)_2, \text{p-OH, p-OCH}_3, \text{p-CH}_3, \text{o-NO}_2, \text{m-NO}_2, \text{p-NO}_2}
\]

The efficient and environmentally friendly synthesis of chalcones and 2,6-bis(arylmethylidene) cycloalkanones is carried out by aldol condensation of ketones with aromatic aldehydes in water in the presence of polyethylene glycol 400 (Tanemura et al. 2005). Saxena et al. (2007) synthesized chalcone derivatives on estradiol framework which shows potent activity against some human cancer cell lines (Scheme-7).
A series of 3,5-bis(arylidene)-4-piperidones I (R = 4-NO2C6H4, 2-thienyl, 4-MeC6H4, etc.), as chalcone analogs carrying variety of aryl and heteroaryl groups, pyrazolo[4,3-c]pyridines II (R = 4-MeC6H4, 2-thienyl, 4-MeOC6H4, R’ = Me, Ph), pyrido[4,3-d]pyrimidines III, and pyrido[3,2-c]pyridines IV, carrying an arylidene moiety, and a series of pyrano[3,2-c]pyridines V, as flavone and coumarin isosteres, were synthesized and screened for their in vitro antiviral and antitumor activities. The pyrano[3,2-c]pyridines heterocyclic system proved to be the most active antitumors among the investigated heterocycles.

3. BIOLOGICAL ACTIVITIES OF CHALCONES

Chalcone is an aromatic ketone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones. Some chalcones demonstrated the ability to block voltage dependent potassium channels (Yarishkin et al. 2008). They are intermediates in the biosynthesis of flavonoids, which are substances wide spread in plants and with an array of biological activities. Chalcones are also intermediates in the Auwers synthesis of flavones. Chalcones, considered as the precursors of flavonoids and isoflavones, are also known to be effective antimicrobial activity (Tsukiyama et al. 2002, Friss-Möller et al. 2002, Fukai et al.

Recently, bacterial resistance to antimicrobial agents has resulted in serious public health problems. Several different mechanisms have been put forward for the development of bacterial resistance. These mechanisms of resistance can be specific for an antibiotic or a family of antibiotics or can be non specific. There are more general mechanisms of drug resistance also in which access of the antibiotic into the cell is prevented or reduced by decreasing the transport of the antibiotic into the cell or by increasing the efflux of the drug from the cell to outside medium by efflux pumps. Efflux pumps are found in both Gram-positive and negative pathogens and some of these drug pumps confer multiple-drug resistance (MDR) and the NorA protein of Staphylococcus aureus is one of such pumps (Prasad et al. 2007, Memurry et al. 1980). NorA is a member of the major facilitator superfamily (MFS) of transport proteins, one of the most studied MDR pumps. Its substrates include antimicrobial agents such as ciprofloxacin, norfloxacin and dyes like ethidium bromide and acriflavine (Li and Nikaido 2004). Chalcones have been found to potentiate the activity of berberine, erythromycin and tetracycline, demonstrating a mode of action consistent with inhibition of the NorA MDR efflux pump in S. aureus (Poole 2005).

Methyl hydroxy chalcone (MCHP), found in cinnamon, was thought to be an insulin mimetic, improving insulin response of diabetics (Jarvill-Taylor et al. 2001). It has since been determined that a flavonoid is responsible for the insulin-like biological activity (Anderson 2004).

The chalcones were reported to show potent toxicity to several cancer cells lines and interact with tubulin at its colchicine-binding site. Cancer is the second-leading cause of human deaths in the developing as well as advanced countries. Cancer, a class of diseases, in which a group of cells display uncontrolled growth, invasion and sometimes metastasis. These three malignant properties of cancers differentiate them from benign tumors, which are self-limiting, and do not invade or metastasize. Most cancers form a tumor but some, like leukemia, do not. Cancer affects people at all ages with the risk for most types increasing with age. Cancer caused about 13% of all human deaths in 2007 (7.6 million). Abnormalities in the genetic material of the
transformed cells is one of the most common causes of cancer (Kinzler and Vogelstein 2002). Cancers are classified by the type of cell that resembles the tumor and, therefore, the tissue presumed to be the origin of the tumor. Examples of general categories include Carcinoma, Sarcoma, Germ cell tumor, Blastic tumor or blastoma, Lymphoma and leukemia. Microtubules are essential components of cell structure and are involved in many cellular processes, including mitosis, morphogenesis, intracellular transport and secretion (Han et al. 1998). They are hollow tubes consisting of α- and β-tubulin heterodimers that polymerize parallel to the cylindrical axis. Tubulin binding molecules interfere with the dynamic instability of microtubules and thereby disrupt microtubule inducing cell cycle arrest in the M-phase, forming abnormal spindles and finally leading to apoptotic cell death (Jordan et al. 1998). A variety of natural compounds such as paclitaxol, vinblastin, combretastatin A-4 and colchicine attack microtubules by interfering with the dynamics of tubulin polymerization and depolymerization, resulting in mitotic arrest (Hamel 1996).

Chalcones obtained by convenient synthetic methods strongly inhibit the polymerization of tubulin by binding to the colchicine-binding site. The relatively simple structure and high affinity of chalcones for the colchicine-binding site because of similarity of the two-aryl group placements in the two molecules has led to the synthesis and subsequent evaluation of a large number of chalcones. There are many therapeutic strategies including chemotherapy and radiotherapy for the treatment of this dreadful disease. Because of high systemic toxicity and drug resistance, rate of successful outcomes is quite low in most of the cases. So, there is a strong need of development of novel treatment and prevention approaches for cancer therapy. Among naturally-occurring chalcones and their synthetic analogues (Achanta et al. 2006, Romagnoli et al. 2008, Echeverria et al. 2009, Szliszka et al. 2010, Ilango et al. 2010), several compounds have been found to have cytotoxic activity (antimitotic, a cell growth inhibitor) towards cultured tumor cells.

Free radicals including the superoxide, hydroxyl, hydrogen peroxide and lipid peroxide have been implicated in a number of disease processes. Chalcones are known to possess antioxidant character at various extents. Activated macrophages play a key role in inflammatory responses and release a variety of mediators including nitric oxide (NO). NO is a potent vasodilator that
facilitates leukocytic migration and formation of edema as well as leukocytic activity and cytokine production (Belofsky et. al. 2004). The compounds with the backbone of chalcones have been also reported to possess various biological activities such as anti-inflammatory (Hsieh et al. 2000), analgesic (Viana et al. 2003), antiplatelet (Zhao 2005), antiulcerative (Mukarami et al. 1991), anti malarial (Dominguez et al. 2005), anti-viral (Trivedi et al. 2007) and anti leishmanial (Nielsen et al. 1995).

4. RESULT AND DISCUSSION

4.1. CHEMISTRY

In the present investigation, thirty six chalcone like molecules viz. (E)-3-(substitutedphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-ones (1-20) and (E)-3-(substitutedphenyl)-(1-furan-2-yl) prop-2-en-1-ones (21-36) have been synthesized by Claisen–Schmidt’s condensation of 2-acetylfuran/2-acetylpyrrol with substituted benzaldehydes under basic conditions (Scheme-8). The synthesized chemical entities (1-36) with diversification in chemical structures are shown in Table 1.

Scheme-8. Synthesis of (E)-3-(substitutedphenyl)-1-heterylprop-2-en-1-ones by Claisen–Schmidt condensation of 2-acetyl furan/2-acetylpyrrole with substituted benzaldehydes. Substituent’s of aldehyde and products (1-36) are provided in Table-2.
### Table -2: Chemical entities (1-36) with diversification in chemical structures.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substitutions</th>
<th>Yield (%)</th>
<th>Reaction time (hr)</th>
<th>Mp. (°C)</th>
</tr>
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<tr>
<td>1</td>
<td>NH H</td>
<td>68.8</td>
<td>15</td>
<td>195.8</td>
</tr>
<tr>
<td>2</td>
<td>NH H NO₂</td>
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<td>15</td>
<td>205.3</td>
</tr>
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<td>3</td>
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<td>15</td>
<td>172.4</td>
</tr>
<tr>
<td>4</td>
<td>NH OCH₃ OCH₃ H H</td>
<td>45.45</td>
<td>15</td>
<td>107.2</td>
</tr>
<tr>
<td>5</td>
<td>NH Cl Cl</td>
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<td>15</td>
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</tr>
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<td>7</td>
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<td>24</td>
<td>203.8</td>
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<tr>
<td>8</td>
<td>NH OCH₃ H H H OCH₃</td>
<td>71.0</td>
<td>15</td>
<td>128.7</td>
</tr>
<tr>
<td>9</td>
<td>NH Br H H</td>
<td>62.50</td>
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</tr>
<tr>
<td>10</td>
<td>NH H F H</td>
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<td>15</td>
<td>139.6</td>
</tr>
<tr>
<td>11</td>
<td>NH Cl H Cl</td>
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<td>18</td>
<td>116.0</td>
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<tr>
<td>12</td>
<td>NH H H N(CH₃)₂ H H</td>
<td>70.00</td>
<td>24</td>
<td>203.8</td>
</tr>
<tr>
<td>13</td>
<td>NH OCH₃ H H H OCH₃</td>
<td>71.0</td>
<td>15</td>
<td>128.7</td>
</tr>
<tr>
<td>14</td>
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<td>48</td>
<td>228.5</td>
</tr>
<tr>
<td>15</td>
<td>NH Cl H H Cl</td>
<td>90</td>
<td>24</td>
<td>116.0</td>
</tr>
<tr>
<td>16</td>
<td>NH Cl H Br H</td>
<td>87.5</td>
<td>15</td>
<td>178.5</td>
</tr>
<tr>
<td>17</td>
<td>NH OCH₃ H OCH₃ H H</td>
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<td>18</td>
<td>105.1</td>
</tr>
<tr>
<td>18</td>
<td>NH H H OCH₃ H H</td>
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<td>20</td>
<td>137.2</td>
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<tr>
<td>19</td>
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</tr>
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<td>15</td>
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<td>21</td>
<td>NH Cl H H Cl</td>
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<td>15</td>
<td>166.4</td>
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<td>22</td>
<td>NH Cl H H Cl</td>
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<td>22</td>
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</tr>
<tr>
<td>24</td>
<td>NH Cl H H Cl</td>
<td>90</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>25</td>
<td>NH Cl H H Cl</td>
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<td>15</td>
<td>88.9</td>
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<td>NH Cl H H Cl</td>
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<td>18</td>
<td>181.2</td>
</tr>
<tr>
<td>27</td>
<td>NH Cl H H Cl</td>
<td>55.5</td>
<td>24</td>
<td>87.5</td>
</tr>
<tr>
<td>28</td>
<td>NH Cl H H Cl</td>
<td>90</td>
<td>48</td>
<td>184.9</td>
</tr>
<tr>
<td>29</td>
<td>NH Cl H H Cl</td>
<td>75</td>
<td>15</td>
<td>67.5</td>
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<tr>
<td>30</td>
<td>NH Cl H H Cl</td>
<td>67</td>
<td>15</td>
<td>180</td>
</tr>
<tr>
<td>31</td>
<td>NH Cl H H Cl</td>
<td>43</td>
<td>24</td>
<td>109.5</td>
</tr>
<tr>
<td>32</td>
<td>NH Cl H H Cl</td>
<td>80</td>
<td>15</td>
<td>230.6</td>
</tr>
<tr>
<td>33</td>
<td>NH Cl H H Cl</td>
<td>89</td>
<td>15</td>
<td>131.6</td>
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<td>34</td>
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<td>NH Cl H H Cl</td>
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<td>10</td>
<td>149.6</td>
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<tr>
<td>36</td>
<td>NH Cl H H Cl</td>
<td>30</td>
<td>18</td>
<td>54</td>
</tr>
</tbody>
</table>
All the compounds were chemically characterized based on their spectral and physical data. Literature search revealed that out of 36 molecules synthesized, compounds 5, 6, 7, 9, 13, 14, 27-29 and 36 are new to literature.

Structure of compound 9 was further confirmed by X-ray analysis of single crystal.

Fig. 1: ORTEP view of the molecule 9 with displacement ellipsoids drawn at 50% probability level. H atoms are shown as small spheres of arbitrary radii. The broken lines show the intramolecular C-H…O, C-H…Br hydrogen bonds.

The crystal used for data collection was of dimension 0.3 x 0.2 x 0.1 mm. The cell dimensions were determined by least-square fit of angular settings of 2440 reflections in the θ range 2.59 to 27.45° Table 3.

Table-3: Crystal data and other experimental details of compound 9.

<table>
<thead>
<tr>
<th>CCDC Number</th>
<th>776070</th>
</tr>
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<tbody>
<tr>
<td>Crystal description</td>
<td>Yellow plate</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.3 x 0.2 x 0.1 mm</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C_{13} H_{10} Br N O</td>
</tr>
<tr>
<td>Formula weight</td>
<td>276.13</td>
</tr>
<tr>
<td>Radiation, Wavelength</td>
<td>Mo Kα, 0.71073 Å</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 31.524(11), b=7.266(2), c=10.000(3) Å, β = 93.171(9)°</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
</tbody>
</table>
Selected bond distances and bond angles are listed in Table 4. An ORTEP view of compound 9 with atomic labeling is shown in Fig. 1 (Radwan and Abbas 2009).

Table 4: Selected bond lengths (Å) and bond angles (°) for non hydrogen atoms (e.s.d.’s are given in parentheses)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length (Å)</th>
<th>Bond</th>
<th>Length (Å)</th>
<th>Bond</th>
<th>Length (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br1-C2&quot;</td>
<td>1.905(2)</td>
<td>O1-C1</td>
<td>1.241(3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.482(3)</td>
<td>C2-C3</td>
<td>1.340(4)</td>
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<td></td>
</tr>
<tr>
<td>N1'-C5'</td>
<td>1.345(3)</td>
<td>N1'-C2'</td>
<td>1.378(3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O1-C1-C2</td>
<td>120.8(2)</td>
<td>C3-C2-C1</td>
<td>119.3(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5'-N1'-C2'</td>
<td>110.4(2)</td>
<td>N1'-C2'-C3'</td>
<td>106.3(2)</td>
<td></td>
<td></td>
</tr>
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<td>N1'-C2'-C1</td>
<td>121.7(2)</td>
<td>N1'-C5'-C4'</td>
<td>108.3(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3&quot;-C2&quot;-Br1</td>
<td>116.5(2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chapter-4  

Synthesis of Chalcones analogs.

The geometry of the molecule was calculated using the WinGX and PARST software (Farrugia 1997, Farrugia 1999). Bond lengths and bond angles of the title molecule show a fair amount of agreement with some related molecules (Nardelli 2005, Li 2008, Tang et al. 2008). The six C-C bond lengths in the phenyl ring lie in the range 1.381(4)-1.408(3) Å. The bond angles in the phenyl ring vary from 116.4(2) to 122.7(2)° with an average of 120.0(2)°. In the title molecule, the bond lengths N1’-C5’ and N1’-C2’ are 1.345(3) and 1.378(3) Å, respectively. The C1=O1 distance [1.241(3) Å] is significantly longer than those usually observed for carbonyl bonds probably because atom O1 is involved in intra-molecular C-H…O hydrogen bond (Table 5).

Table- 5: Hydrogen–bonding geometry (e.s.d.’s in parentheses)

<table>
<thead>
<tr>
<th>D–H…A</th>
<th>D–H(Å)</th>
<th>H…A(Å)</th>
<th>D…A(Å)</th>
<th>D–H…A(°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3-H3...Br1</td>
<td>1.00(2)</td>
<td>2.76(2)</td>
<td>3.187(3)</td>
<td>106(1)</td>
</tr>
<tr>
<td>C3-H3...O1</td>
<td>1.00(2)</td>
<td>2.43(2)</td>
<td>2.798(3)</td>
<td>101(2)</td>
</tr>
<tr>
<td>N1’-H1’…O1i</td>
<td>0.74(3)</td>
<td>2.11(3)</td>
<td>2.824(3)</td>
<td>162(3)</td>
</tr>
</tbody>
</table>

Symmetry code: (i) 1/2-x, 1/2-y, 2-z

The pyrrole and phenyl rings are perfectly planar (maximum deviations: 0.006(2) Å for C5’ and 0.010(2) Å for C1”, respectively). Differently to most substituted chalcones, the molecule of the title compound is non-planar with a dihedral angle of 35.16 (8)° between the pyrrole and phenyl rings (Jasinski et.al., 2009 ). The angles between the mean plane of the prop-2-en-1-one group and the mean planes of the pyrrole and phenyl rings are 15.7 (1) and 30.7(1)°, respectively. In the crystal structure, intermolecular N1’-H1’…O1 hydrogen bond links the molecules into centrosymmetric dimers (Fig. 2). Dimers are arranged in a manner to form layers (Fig. 3). Within the layers, the dimers are arranged parallel to each other.
Fig. 2: Plot of two molecules of 9 showing intermolecular N-H…O hydrogen bonds.

Fig. 3: Appearance of layers of dimers of the compound 9 that are hydrogen bonded.
4.2. BIOLOGICAL EVALUATION

4.2.1 In vitro combination study of ciprofloxacin with molecules (1-36)

The MIC of the compounds (1-36) was determined to use these molecules at concentration devoid of antibacterial activity, a prerequisite of any compound to be used as safe efflux pump inhibitors (EPIs). The compounds (1-36) were studied in combination with ciprofloxacin (standard drug) and bio-evaluated against Nor A over expressing S. aureus 1199B (Bandgar et al. 2008, Kaatz et al. 1993, Kaatz et al. 1999). Along with these synthetic molecules, two known efflux pump inhibitors namely reserpine and verapamil were also used for the comparative studies (Kaatz and Seo 1995, Neyfakh et al. 1993). Ciprofloxacin alone showed MIC at 8 µg/mL against NorA over expressing S. aureus 1199B. Among the library of 36 molecules used in combination with ciprofloxacin and tested against S. aureus 1199B, only compounds 5, 9, 10, 15, 17, 18, 25, 29 and 33 could reduce the MIC of the drug (Table-6) and rest of the molecules failed to potentiate the antibacterial activity of the drug. However, the compounds 5, 15, 29, 25 and 33, showed the reduction of MIC of ciprofloxacin by fourfold and the rest of the active compounds indicated two-fold reduction in the MIC of ciprofloxacin. Compound 25 was found to be the most active compound in this study, which showed fourfold reduction in the MIC of ciprofloxacin at 12.5 µg/mL conc. against S. aureus 1199B.

Table-6: Ciprofloxacin activity against S. aureus 1199B in combination with (E)-3-(substitutedphenyl) -1-hetarylprop-2-en-1-ones(1-36).

<table>
<thead>
<tr>
<th>Compound</th>
<th>MEC&lt;sup&gt;a&lt;/sup&gt; of compounds</th>
<th>MIC&lt;sup&gt;b&lt;/sup&gt; of ciprofloxacin (µg/mL) Without EPI</th>
<th>With EPI</th>
<th>Fold reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;50</td>
<td>8</td>
<td>8</td>
<td>0</td>
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<tr>
<td>14</td>
<td>&gt;50</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>25</td>
<td>8</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>
### 4.2.2. Anticancer activity

Among the currently identified anti-tumor agents, chalcones represent an important class of molecules that are abundant in edible plants. The anticancer activity of certain chalcones is believed to be a result of binding to tubulin and preventing it from polymerizing into microtubules (Seral et al. 2001). The prepared synthetics (1-36) were also evaluated for their anticancer activity against four different cancer cell lines (HL-60, MOLT-4, PC-3 and HeLa). Out of 36, 14 molecules showed significant anticancer activity (Table-7). Compound 25 having -N(CH₃)₂ substitution at ring A (R₃) was the most active. Compounds 11, 21, 24 having chloro substitution at different positions in ring A of (E)-3-(substitutedphenyl)-1-hetylprop-2-en-1-ones also showed promising anticancer activity.
Table- 7: List of IC₅₀ values (µM) of active compounds in four human cancer cell lines.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>HL-60</th>
<th>PC-3</th>
<th>MOLT-4</th>
<th>Hela</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>&gt;100</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>8</td>
<td>16</td>
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</tr>
<tr>
<td>9</td>
<td>42</td>
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<td>38</td>
<td>44</td>
</tr>
<tr>
<td>11</td>
<td>13</td>
<td>18</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>14</td>
<td>38</td>
<td>55</td>
<td>42</td>
<td>68</td>
</tr>
<tr>
<td>16</td>
<td>32</td>
<td>44</td>
<td>49</td>
<td>&gt;100</td>
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<td>21</td>
<td>12</td>
<td>14</td>
<td>25</td>
<td>26</td>
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<td>38</td>
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<tr>
<td>28</td>
<td>58</td>
<td>62</td>
<td>72</td>
<td>&gt;100</td>
</tr>
<tr>
<td>33</td>
<td>48</td>
<td>58</td>
<td>62</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

Compounds 2, 3, 26 having nitro substitution in ring A also exhibited promising anticancer activity, while compounds 14 and 28 having both nitro and chloro substitutions in ring A of (E)-3-(substitutedphenyl)-1-heterylprop-2-en-1-ones were less active. Compounds without any modification in these rings did not show any anticancer activity (1 and 27).

4.2.3. Anti-inflammatory and anti-oxidant activity

Anti-inflammatory and antioxidant activities of all the synthesized molecules were determined by using carrageenan induced inflammation and DPPH methods respectively. Out of the 36 synthetics tested, except compound 31 which showed mild anti-inflammatory activity at 100 mg/kg p.o. (23% inhibition), others were devoid of activity.

5. MOLECULAR DOCKING STUDY

A flexible docking study was performed in order to rationalize the observed cytotoxic activity of compound 25. GOLD software was employed for this purpose and Goldscore was used to score the binding conformations. The coordinates of the colchicine-binding site of tubulin receptor were obtained from a protein data bank (PDB ID: 1SA0) (Ravelli et al. 2004) on which docking was performed. To validate that the docking procedure for the prediction of the correct binding
mode of ligands at the colchicine-binding site, colchicine was extracted from the original crystal structure (1SA0) and re-docked using GOLD. The highest scoring conformation was selected and compared with crystal structure conformation based on RMSD (0.72 Å).

The best binding conformation of the compound 25 in a colchicine-binding site was selected based on the GOLD score and visual inspection. In the binding conformation, compound 25 fits well in the binding cavity of colchicine (Fig. 4). Oxygen of the furan ring is involved in important hydrogen bonding interaction with Met 259, which acts as anchor to hold the compound in the cavity. Moreover, phenyl ring of compound 25 finds optimum position over the Lys254 and Leu2 Leu255, and the dimethyl amine is present in vicinity to the Asn101 and Asn249.

![Fig. 4: Docking conformation of compound 25 at colchicine-binding site of tubulin receptor.](image)

6. CONCLUSION

Preparations of a series of chalcone like derivatives having B ring either as pyrrole or furan and their biological activities are described. Compounds 11, 21, 25 and 26 were found to have good anticancer activity in all four tested cancer cell lines (HL-60, MOLT-4, PC-3 and HeLa) while compounds 5, 9, 10, 15, 17, 18, 25, 29 and 33 were identified as efflux pump inhibitors against S. aureus. Compounds with methoxy substitution did not reveal any significant activity. Molecules
1-36 possess insignificant antioxidant and anti-inflammatory activities. The result of this study finds compound 25 as lead molecule towards the development of new therapeutic agent to fight cancer as well as NorA efflux pump inhibitor.

7. EXPERIMENTAL

7.1 Materials and methods

Reagents for chemical synthesis were obtained from Sigma-Aldrich. The solvents used in reactions were distilled and dried before use. Reactions were monitored by TLC on 0.25 mm silica gel 60 F254 plates (E. Merck) using UV light, or ceric ammonium sulfate solution for visualization of the spots. Melting points were recorded on Buchi-510 instrument and elemental analyses were performed on Elementar vario EL-III. 1H NMR & 13C NMR spectra were recorded on Bruker DPX 200/400/500 instruments using CD3OD/CDCl3/DMSO-d6 as solvent with TMS as internal standard. Mass spectra were recorded on ESI-esquire 3000 Bruker Daltonic's instrument and IR spectra were recorded on Bruker Vector 22 instruments. X-ray intensity data was collected at 100K on Bruker CCD area-detector diffractometer equipped with graphite monochromated MoKα radiation.

7.2 General procedure for synthesis of chalcone like (E)-3-(substitutedphenyl)-1-hetarylprop-2-en-1-ones (1-36)

2-Acetylpyrrole/2-acetylfuran (4 mmol) was taken in a flask (100 mL) and dissolved in 10 mL methanol. Substituted benzaldehyde (4 mmol) was added to the solution followed by 10% aqueous NaOH solution (2 mL) and the reaction mixture was kept in stirred condition at 15-20°C until completion of the reaction. Progress of the reaction was monitored by TLC (7:3, n-hexan: acetone). Spots on TLC were visualized by spraying with 2% ceric ammonium sulfate spray reagent followed by heating the plate at 120°C. After completion of the reaction, mixture was diluted with distilled water and allowed to stand at room temperature for precipitation. Precipitated solid was filtered and re-crystallized from EtOH/EtOAc. Melting point, reaction time and yield of the products are shown in Table-2. The purity of products was monitored on TLC (30% acetone in n-hexane).
**SPECTRAL DATA AND ELEMENTAL ANALYSIS OF SYNTHESIZED MOLECULES.**

*(E)-3-Phenyl-1-(1H-pyrrol-2-yl)prop-2-en-1-one (1)*

MS: $M^+$ at $m/z$ 197; Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10%. Found: C, 79.28; H, 5.60; N, 7.25%. $^1H$ NMR (200 MHz, CD$_3$OD): $\delta$ 6.32 (dd, 1H, $J = 2.4$ Hz and 3.8 Hz, H-4'), 7.19 (d, 1H, $J = 15.0$ Hz, H-2), 7.34 (m, 5H, H-2”, H-3”, H-4”, H-5” and H-6”), 7.45 (d, 1H, $J = 15.0$ Hz, H-3), 7.76 (bs, 2H, H-3’ and H-5’), 10.65 (s, 1H, NH); $^{13}C$ NMR (100 MHz, CD$_3$OD): $\delta$ 178.81 (C-1), 140.94 (C-3), 133.12 (C-1”), 131.35 (C-2’), 130.21 (C-3” and C-5”), 130.12 (C-4”), 127.98 (C-5’), 126.08 (C-2” and C-6”), 125.90 (C-3’), 121.88 (C-2), 111.43 (C-4”).

*(E)-3-(4-Nitro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (2)*

MS: $M^+$ at $m/z$ 242; Anal. Calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56%. Found: C, 64.57; H, 4.14; N, 11.67%. $^1H$ NMR (200 MHz, DMSO-d$_6$): $\delta$ 6.34 (dd, 1H, $J = 2.4$ and 3.8 Hz, H-4”), 7.19 (d, 1H, $J = 15.2$ Hz, H-2), 7.34 (d, 1H, $J = 15.2$ Hz, H-3), 7.76 (bs, 2H, H-3’ and H-5”), 7.79 (d, 2H, $J = 8.8$ Hz, H-2” and H-6”), 8.79 (d, 2H, $J = 8.8$ Hz, H-3” and H-5”), 9.50 (s, 1H, H-1’, NH); $^{13}C$ NMR (100 MHz, DMSO-d$_6$): 178.10 (C-1), 162.49, (C-4”), 142.46 (C-3), 140.18 (C-2’), 133.15 (C-1”), 128.42 (C-2” and C-6”), 128.02 (C-5”), 125.73 (C-3’), 120.6 (C-2), 120.58 (C-3” and C-5”), 111.97 (C-4”).

*(E)-3-(3-Nitrophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (3)*

MS: $M^+$ at $m/z$ 242; Anal. Calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56%. Found: C, 64.38; H, 4.70; N, 11.67%. $^1H$ NMR (200 MHz, DMSO-d$_6$): $\delta$ 6.31 (bs, 1H, H-4”), 7.21 (bs, 1H, H-3”), 7.48 (bs, 1H, H-5”), 7.72 (dd, $J = 8.52$ Hz and 8.04 Hz, H-5”), 7.74 (dd, 1H, $J = 16.00$ Hz, H-2), 7.92 (dd, 1H, $J = 16$ Hz, H-3), 8.28 (m, 2H, H-4” and H-6”), 8.72 (s, 1H, H-2”), 9.65 (s, 1H, H-1’, NH); $^{13}C$ NMR (125 MHz, DMSO-d$_6$): 178.10 (C-1), 149.46 (C-3”), 140.29 (C-3), 135.18 (C-1”), 133.87 (C-6”), 132.15 (C-2’), 129.42 (C-5”), 128.19 (C-5’), 125.73 (C-3’), 122.19 (C-2), 122.92 (C-2”), 120.69 (C-4”), 112.91 (C-4”).
(E)-3-(2,4-Dichloro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (4)

MS: M⁺ at m/z 266; Anal. Calcd for C₁₃H₉Cl₂NO: C, 58.67; H, 3.41; N, 5.26 %. Found: C, 58.76; H, 4.45; N, 5.38 %; ¹H NMR (200 MHz, DMSO-d₆): δ 6.37 (bs, 1H, H-4'), 7.10 (d, 1H, J = 15.60 Hz, H-2), 7.30 (m, 3H, H-5", H-6" and H-3’), 7.47 (d, 1H, J = 1.9 Hz, H-3”), 7.69 (d, 1H, J = 8.60 Hz, H-5”), 8.13 (d, 1H, J = 15.60 Hz, H-3), 10.50 (s, 1H, NH); ¹³C NMR (100 MHz, DMSO-d₆): 178.10 (C-1), 140.38 (C-3), 135.81 (C-4”), 133.65 (C-2”), 133.03 (C-2’), 131.84 (C-3”), 131.23 (C-1”), 130.27 (C-6”), 128.59 (C-5’), 127.89 (C-5”), 126.21 (C-3’), 122.59 (C-2), 115.89 (C-4’).

(E)-3-(2, 3-Dimethoxy-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (5)

MS: M⁺ at m/z 257; Anal. Calcd for C₁₅H₁₅NO₃: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.16; H, 4.92; N, 5.47 %; ¹H NMR (200 MHz, CDCl₃): δ 3.89 (s, 6H, 2×OCH₃), 6.35 (bs, 1H, H-4’), 6.96 (d, 1H, J = 8.22 Hz, H-4”), 7.10 (m, 2H, H-5” and H-6”), 7.28 (m, 2H, H-3’ and H-5”), 7.42 (d, 1H, J = 15.90 Hz, H-2), 8.11 (d, 1H, J = 15.90 Hz, H-3), 10.25 (s, 1H, NH); ¹³C NMR (125 MHz, CDCl₃): 178.10 (C-1), 162.49 (C-3”), 159.40 (C-2”), 145.34 (C-3), 135.98 (C-2’), 129.32 (C-5’), 125.88 (C-3’), 123.24 (C-5”), 122.09 (C-2), 120.00 (C-6”), 116.77 (C-1”), 115.87 (C-4”), 109.94 (C-4’), 55.95 (OCH₃)₂.

(E)-3-(2, 3-Dichloro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (6)

MS: M⁺ at m/z 266. Anal. Calcd for C₁₃H₉Cl₂NO : C, 58.67; H, 3.41; N, 5.26 %. Found: C, 59.72; H, 4.48; N, 5.37 %. ¹H NMR (200 MHz, CD₃OD): δ 6.32 (dd, 1H, J = 2.62 and 3.74 Hz, H-4’), 7.16 (m, 4H, H-3’, H-4”, H-5” and H-6”), 7.23 (m, 1H, H-5’), 7.55 (d, 1H, J = 15.90 Hz, H-2), 8.06 (d, 1H, J = 15.90 Hz, H-3), 10.52 (s, 1H, NH); ¹³C-NMR (125 MHz, CD₃OD): δ 178.28 (C-1), 140.92 (C-3), 135.92 (C-1”), 135.92 (C-3”), 133.42 (C-2”), 131.92 (C-4”), 130.21 (C-5”), 129.37 (C-2’), 128.01 (C-5’), 126.52 (C-6”), 125.95 (C-3’), 122.09 (C-2), 113.05 (C-4’).
(E)-3-(2, 6-Dichloro-phenyl)-1-(1H-pyrro-2-yl)prop-2-en-1-one (7)

MS: M⁺ at m/z 266. Anal. Calcd for C₁₃H₉Cl₂NO: C, 58.67; H, 3.41; N, 5.26 %. Found: C, 59.79; H, 3.18; N, 5.23 %. ¹H-NMR (200 MHz, CD₃OD): δ 6.32 (dd, 1H, J = 2.41 Hz and 3.89 Hz, H-4’), 7.17 (m, 1H, H-3’), 7.31 (d, 1H, J = 15.98 Hz, H-2), 7.55 (m, 3H, H-3”, H-4” and H-5”), 7.75 (bs, 1H, H-5’), 7.87 (d, 1H, J = 15.98 Hz, H-3), 10.25 (s, 1H, H-1’,NH).

¹³C NMR (125 MHz, CD₃OD): δ 179.91 (C-1), 140.59 (C-3), 136.05 (C-1”), 133.16 (C-2” and C-6”), 132.82 (C-2’), 131.5 (C-4”), 128.52 (C-5”), 127.19 (C-3” and C-5”), 126.05 (C-3’), 122.12 (C-2), 112.25 (C-4’).

(E)-3-(3-Methoxyphenyl)-1-(1H-pyrro-2-yl)prop-2-en-1-one (8)

MS: M⁺ at m/z 227. Anal. Calcd for C₁₄H₁₃NO₂: C, 73.99; H, 5.77; N, 6.16 %. Found: C, 74.02; H, 5.81; N, 5.27 %. ¹H NMR (400 MHz, CDCl₃): δ 3.84 (s, 3H, OCH₃), 6.33 (m, 1H, H-4’), 6.94 (dd, 1H, J = 8.00 Hz and 2.04 Hz, H-4”), 7.04 (m, 1H, H-3’), 7.26 (d, 1H, J = 7.79 Hz, H-6”), 7.44 (dd, 1H, J = 8.00 Hz and 7.79 Hz, H-5”), 7.32 (d, 1H, J = 16.00 Hz, H-2), 7.64 (d, 1H, J = 1.6 Hz, H-5’), 7.79 (d, 1H, J = 16.00 Hz, H-3), 10.55 (s, 1H, NH). ¹³C NMR (100 MHz, CDCl₃): 179.06 (C-1), 159.94 (C-3”), 142.21, (C-3), 136.46 (C-1”), 133.16 (C-2”), 129.90 (C-5’), 125.97 (C-3’), 122.47 (C-5”), 120.99, (C-2) 116.99 (C-6”), 115.95 (C-4”), 113.47 (C-4’), 110.94 (C-2”) and 55.34 (OCH₃).

(E)-3-(2-Bromophenyl)-1-(1H-pyrro-2-yl)prop-2-en-1-one (9)

MS: M⁺ at m/z 276. Anal. Calcd for C₁₃H₁₀BrNO: C, 73.99; H, 5.77; N, 6.16 %. Found: C, 74.12; H, 5.78; N, 5.17 %. ¹H NMR (400 MHz, CDCl₃): δ 6.35 (m, 1H, H-4’), 7.09 (m, 1H, H-4”), 7.17 (m, 1H, H-3’), 7.28 (d, 1H, J = 16.00 Hz, H-2), 7.35 (d, 1H, J = 8.70 Hz, H-6”), 7.40 (d, 1H, J = 1.68 Hz, H-5’), 7.62 (dd, 1H, J = 8.70 Hz and 1.60 Hz, H-5”), 7.74 (dd, 1H, J = 8.70 Hz and 1.60Hz, H-3”), 8.18 (d, 1H, J = 16.00 Hz, H-3), 10.5 (bs, 1H, NH). ¹³C NMR (100 MHz, CDCl₃): 178.59 (C-1), 140.61 (C-3), 135.21 (C-1”), 133.48 (C-4”), 132.98 (C-2”), 131.00 (C-3”), 127.82 (C-6”), 127.64 (C-5”), 126.17 (C-5’), 125.74 (C-2), 125.04 (C-3’), 117.01 (C-2”) and 111.04 (C-4’).
(E)-3-(4-Fluorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (10)

MS: M⁺ at m/z 215. Anal. Calcd for C₁₃H₁₀FNO: C, 72.55; H, 4.68; N, 6.51 %. Found: C, 72.65; H, 4.72; N, 6.59 %. ¹H NMR (400 MHz, CDCl₃): δ 6.34 (m, 1H, H-4’), 7.06 (d, 1H, J = 2.03 Hz, H-3’), 7.10 (m, 2H, H-3” and H-5”), 7.16 (m, 1H, H-5’), 7.30 (m, 1H, H-3”), 7.59 (m, 2H, H-2” and H-6”), 7.80 (d, 1H, J = 15.66 Hz, H-3).

¹³C NMR (100 MHz, CDCl₃): 178.81 (C-1), 165.10 (C-4”), 145.01 (C-3), 135.94 (C-2’), 133.12 (C-1”), 130.21 (C-2”), 130.21 (C-6”), 126.08 (C-5’), 121.90 (C-3’), 121.88 (C-2), 116.81 (C-3”), 116.11 (C-5”).

(E)-3-(4-Chlorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (11)

MS: M⁺ at m/z 213.5. Anal. Calcd for C₁₃H₁₀ClNO: C, 67.39; H, 4.35; N, 6.05 %. Found: C, 67.34; H, 4.38; N, 6.13 %. ¹H NMR (400 MHz, CDCl₃): δ 6.36 (m, 1H, H-4’), 7.07 (m, 1H, H-3”), 7.12 (m, 1H, H-5’), 7.31 (d, 1H, J = 15.69 Hz, H-2), 7.54 (d, 2H, J = 8.0 Hz, H-3” and H-5”), 7.59 (d, 2H, J = 8 Hz, H-2” and H-6”), 7.75 (d, 1H, J = 15.6 Hz, H-3), 9.73 (bs, 1H, H-1’ (NH)).

¹³C NMR (100 MHz, CDCl₃): 178.67 (C-1), 140.79 (C-3), 136.04 (C-4”), 133.56 (C-1”), 133.08 (C-2’), 132.94 (C-5’), 129.17 (C-3” and C-5”), 129.09 (C-2” and C-6”), 125.85 (C-3”), 116.51 (C-4”).

(E)-3-(4-Dimethylaminophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (12)

MS: M⁺ at m/z 240. Anal. Calcd for C₁₅H₁₆N₂O: C, 74.97; H, 6.71; N, 11.66 %. Found: C, 75.85; H, 6.78; N, 11.68 %. ¹H NMR (500 MHz, CDCl₃): δ 3.05 (s, 6H, -N(CH₃)₂), 6.33 (m, 1H, H-4”), 6.70 (d, 2H, J = 8.8 Hz, H-3” & H-5”), 7.03 (m, 1H, H-3”), 7.05 (m, 1H, H-5”), 7.17 (d, 1H, J = 15 Hz, H-2), 7.54 (d, 2H, J = 8.8 Hz, H-2” and H-6”), 7.79 (d, 1H, J = 15.5, H-3), 9.55 (s, 1H, H-1’ (-NH)).

¹³C NMR (125 MHz, CDCl₃): δ 179.35 (C-1), 151.85 (C-4”), 143.07 (C-3), 133.58 (C-2”), 130.15 (C-2” and C-6”), 124.54 (C-5’), 122.89 (C-1”), 116.90 (C-3”), 115.26 (C-2), 111.89 (C-3” and C-5”), 110.62 (C-4”), 40.14 (-N(CH₃)₂).
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(E)-3-(2, 6-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (13)

MS: M⁺ at m/z 257. Anal. Calcd for C₁₅H₁₅NO₃: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.16; H, 5.92; N, 6.55 %. ¹H NMR (500 MHz, CDCl₃): δ 3.82 (s, 6H, (-OCH₃)₂), 6.35 (m, 1H, H-4’), 6.91 (d, 1H, J = 16.48 Hz, H-2), 6.94 (dd, 1H, J = 3.02 Hz and 5.9 Hz, H-3’), 7.07 (m, 2H, H-3” and H-5”), 7.16 (t, 1H, J = 3.2 Hz, H-5’), 7.42 (d, 1H, J = 16.48 Hz, H-3), 8.08 (dd, 1H, J = 8.00 Hz , H-4”), 9.65 (s, 1H, NH ). ¹³C NMR (125 MHz, CDCl₃): δ 178.56 (C-1), 150.87 (C-2” and C-6”), 143.48 (C-3), 135.76 (C-4”), 133.17 (C-2’), 129.80 (C-5’), 125.96 (C-3’), 123.87(C-2), 111.98 (C-4”), 110.60 (C-1”), 109.98 (C-3” and C-5”), 55.95 (OCH₃), 55.56 (OCH₃).

(E)-3-(2-Chloro-5-nitrophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (14)

MS: M⁺ at m/z 276.5. Anal. Calcd for C₁₃H₉ClN₂O₃: C, 56.43; H, 3.28; N, 10.13 %. Found: C, 56.56; H, 3.32; N, 10.43 %. ¹H NMR (500 MHz, DMSO-d₆): δ 6.33 (m, 1H, H-4’), 7.25 (s, 1H, H-3’), 7.55 (s, 1H, H-5’), 7.84 (d, 1H, J = 8.8 Hz, H-3”), 7.90 (d, 1H, J = 15.5 Hz, H-2), 8.02 (d, 1H, J = 15.5 Hz, H-3), 8.22 (dd, 1H, J = 2.5 and 8.0 Hz, H-4”), 8.93 (d, 1H, J = 2.5 Hz, H-6”). ¹³C NMR(125 MHz, DMSO-d₆): δ 176.70 (C-1), 146.85 (C-5”), 140.14 (C-3), 134.01 (C-1”), 133.41 (C-2”), 132.80 (C-2’), 131.30 (C-3”), 128.32 (C-5’), 127.31 (C-6”), 125.19 (C-3’), 122.77 (C-2), 118.72 (C-4”), 110.39 (C-4’).

(E)-3-(2-Chlorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (15)

MS: M⁺ at m/z 231.5. Anal. Calcd for C₁₃H₁₀ClN O: C, 67.39; H, 4.35; N, 6.05 %. Found: C, 67.55; H, 4.36; N, 6.08 %. ¹H NMR (500 MHz, CDCl₃): δ 6.35 (m, 1H, H-4”), 7.10 (m, 1H, H-4”), 7.11 (s, 1H, H-5”), 7.18 (s, 1H, H-3”), 7.30 (m, 2H, H-3” and H-6”), 7.34 (d, 1H, J = 15.8 Hz, H-2), 7.74 (m, 1H, H-5’), 8.23 (1H, d, J = 15. 8 Hz, H-3), 10.59 (bs, 1H, NH). ¹³C NMR(125 MHz, CDCl₃): δ 178.68 (C-1), 138.04 (C-3), 135.32 (C-1”), 133.36 (C-2”), 133.00 (C-2”), 130.86 (C-4”), 130.22 (C-3”), 127.70 (C-6”), 127.02 (C-5’), 126.32 (C-5”), 124.77 (C-3’), 117.15 (C-2), 111.02 (C-4’).

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**(E)-3-(4-Bromophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (16)**

MS: M⁺ at m/z 276. Anal. Calcd for C₁₃H₁₀BrNO: C, 56.55; H, 3.65; N, 5.07 %. Found: C, 56.59; H, 3.68; N, 5.17 %.

**1H NMR (500 MHz, DMSO-d₆):** δ 6.31 (m, 1H, H-4'), 7.21 (dd, 1H, J = 1.47 and 0.56 Hz, H-3'), 7.42 (dd, 1H, J = 1.11 and 2.6 Hz, H-5'), 7.64 (d, 1H, J = 15.76 Hz, H-2), 7.65 (d, 2H, J = 8.36 Hz, H-2" and H-6''), 7.76 (d, 1H, J = 15.7 Hz, H-3), 7.83 (d, 2H, J = 8.36 Hz, H-3" and H-5''), 10.59 (bs, 1H, NH).

**13C NMR (125 MHz, DMSO-d₆):** δ 177.49 (C-1), 139.28 (C-3), 134.08 (C-1''), 131.74 (C-3' and C-5''), 130.35 (C-2' and C-6''), 126.60 (C-5''), 123.75 (C-3''), 123.29 (C-4''), 117.62 (C-2), 110.22 (C-4').

**(E)-3-(2,4-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (17)**

MS: M⁺ at m/z 257. Anal. Calcd for C₁₅H₁₃NO₃: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.12; H, 5.91; N, 5.51 %.

**1H NMR (500 MHz, DMSO-d₆):** δ 3.84 (s, 6H, (OCH₃)₂), 6.26 (m, 1H, H-4'), 6.63 (m, 2H, H-3'' and H-5''), 7.14 (m, 1H, H-3'), 7.27 (dd, 1H, J = 1.05 and 2.5 Hz, H-5''), 7.54 (d, 1H, J = 15.77 Hz, H-2), 7.37 (d, 1H, J = 8.52 Hz, H-6''), 7.92 (d, 1H, J = 15.77 Hz, H-3), 10.55 (s, 1H, NH). **13C NMR (125 MHz, DMSO-d₆):** δ 178.10 (C-1), 162.49 (C-4''), 159.46 (C-2''), 135.18 (C-3), 133.15 (C-2''), 129.42 (C-5''), 125.73 (C-3''), 120.06 (C-6''), 116.47 (C-2), 115.97 (C-4''), 109.91 (C-1''), 106.09 (C-5''), 98.16 (C-3''), 55.86 (OCH₃), 55.71 (OCH₃).

**(E)-3-(4-Methoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (18)**

MS: M⁺ at m/z 228. Anal. Calcd for C₁₄H₁₃NO₂: C, 73.99; H, 5.77; N, 6.11 %. Found: C, 74.03; H, 5.80; N, 6.15 %.

**1H NMR (500 MHz, CDCl₃):** δ 3.90 (s, 3H, OCH₃), 6.35 (m, 1H, H-4''), 6.94 (d, 2H, J = 8.76 Hz, H-3'' and H-5''), 7.06 (m, 1H, H-3''), 7.09 (m, 1H, H-5''), 7.25 (d, 1H, J = 15.67, H-2), 7.60 (d, 2H, J = 8.76 Hz, H-2'' and H-6''), 7.81 (d, 1H, J = 15.67, H-3), 10.59 (s, 1H, NH). **13C NMR (125 MHz, CDCl₃):** δ 178.28 (C-1), 163.48 (C-4''), 136.21 (C-3), 133.49 (C-2''), 131.92 (C-2' and C-6''), 128.56 (C-1''), 127.58 (C-5''), 125.98 (C-3''), 120.06 (C-2), 118.89 (C-3' and C-5''), 115.82 (C-4''), 55.71 (OCH₃).
(E)-3-(3, 4-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (19)

MS: M⁺ at m/z 258. Anal. Calcd for C₁₅H₁₅NO₃: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.12; H, 5.92; N, 5.51 %.

1H NMR (500 MHz, DMSO-d₆): δ 3.86 (s, 6H, OCH₃₂), 6.27 (d, 1H, J = 2.45 Hz, H-4’), 7.01 (d, 1H, J = 8.35 Hz, H-5’), 7.15 (s, 1H, H-2’), 7.35 (dd, 1H, J = 1.83 and 8.35 Hz, H-6’), 7.38 (m, 1H, H-3’), 7.48 (d, 1H, J = 1.74 Hz, 5’), 7.56 (d, 1H, J = 15.84 Hz, H-2), 7.64 (1H, d, J = 15.84 Hz, H-3), 10.55 (s, 1H, NH).

13C NMR (125 MHz, DMSO-d₆): δ 177.83 (C-1), 150.68 (C-3’), 148.8 (C-4’), 140.98 (C-3), 133.07 (C-2’), 127.60 (C-1”), 125.94 (C-5’), 123.07 (C-3’), 120.60 (C-2), 116.96 (C-6”), 111.44 (C-5”), 110.50 (C-4’), 109.88 (C-2”), 55.59 (OCH₃), 55.45 (OCH₃).

(E)-3-(Benzo[d][1, 3]dioxol-6-yl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (20)

MS: M⁺ at m/z 242. Anal. Calcd for C₁₄H₁₁NO₃: C, 69.70; H, 4.60; N, 5.81 %. Found: C, 69.79; H, 4.67; N, 5.89 %.

1H NMR (500 MHz, CDCl₃): δ 6.03 (s, 2H, O-CH₂-O), 6.35 (m, 1H, H-4’), 6.98 (m, 1H, H-3”), 7.13 (d, 1H, J = 8.04 Hz, H-5’), 7.18 (d, 1H, J = 15.62 Hz, H-2), 7.74 (d, 1H, J = 15.62 Hz, H-3) 10.55 (s, 1H, NH).

13C NMR (125 MHz, CDCl₃): δ 177.89 (C-1), 152.59 (C-2’), 152.09 (C-4”), 52.05 (C-1’), 140.9 (C-3), 133.24 (C-2”), 128.28 (C-5’), 126.29 (C-3”), 123.95, (C-5”), 123.05 (C-2), 120.89 (C-6”), 118.52 (C-1”), 115.92 (C-4’), 102.61 (OCO).

(E)-3-(2-Chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one (21)

MS: M⁺ at m/z 232.5. Anal. Calcd for C₁₃H₉ClO₂: C, 67.11; H, 3.90 %. Found: C, 67.20; H, 3.89 %.

1H NMR (400 MHz, CDCl₃): δ 6.61 (dd, 1H, J = 1.8 & 3.5 Hz, H-4’), 7.21 (m, 3H, H-4”’, H-5” and H-3’), 7.37 (m, 2H, H-3”’, H-6”), 7.58 (d, 1H, J = 16.04 Hz, H-2), 7.78 (bs, 1H, H-5”), 7.95 (d, 1H, J = 16.04 Hz, H-3).13C NMR (100 MHz, CDCl₃): δ 177.25 (C-1), 153.63 (C-2’), 149.82 (C-5”), 140.23 (C-3), 133.25 (C-2”), 133.07 (C-1”), 132.05 (C-4”), 131.83 (C-3”), 128.52 (C-6”), 127.76 (C-5”), 122.52 (C-2), 122.12 (C-3’), 112.6 (C-4’).
(E)-3-(2-Bromophenyl)-1-(furan-2-yl)prop-2-en-1-one (22)

MS: M⁺ at m/z 277. Anal. Calcd for C₁₃H₉BrO₂: C, 56.34; H, 3.27 %. Found: C, 56.42; H, 3.29 %. ¹H-NMR (400 MHz, DMSO-d₆): δ 6.60 (m, 1H, H-4’), 7.35 (m, 1H, H-3’), 7.44 (d, 1H, J = 16.01 Hz, H-2), 7.55 (m, 4H, H-3”, H-4”, H-5” & H-6”), 7.66 (m, 1H, H-5’), 7.84 (d, 1H, J = 16.01 Hz, H-3). ¹³C NMR (100 MHz, DMSO-d₆): δ 177.73 (C-1), 153.62 (C-2’), 146.63 (C-5’), 142.53 (C-3), 135.80 (C-1”), 133.66 (C-4”), 132.21 (C-3”), 129.87 (C-6”), 129.04 (C-5”), 124.89 (C-2”), 121.71 (C-2), 121.24 (C-3’), 112.66 (C-4’).

(E)-3-(4-fluorophenyl)-1-(furan-2-yl)prop-2-en-1-one (23)

MS: M⁺ at m/z 216. Anal. Calcd for C₁₃H₉FO₂: C, 72.22; H, 4.20 %. Found: C, 73.38; H, 4.19 %. ¹H-NMR (500 MHz, CDCl₃): δ 6.59 (m, 1H, H-4’), 7.09 (d, 1H, J = 8.62 Hz, H-3”), 7.11 (d, 1H, J = 8.62 Hz, H-2”), 7.63 (d, 1H, J = 8.62 Hz, H-6”), 7.65 (d, 1H, J = 1.64 Hz, H-5”), 7.83 (d, 1H, J = 15.76 Hz, H-3). ¹³C NMR (500 MHz, CDCl₃): δ 177.73 (C-1), 165.08 (C-4”), 153.61 (C-2’), 146.60 (C-5’), 146.60 (C-3’), 130.98 (C-1”), 130.42 (C-2’ and C-6”), 120.84 (C-2), 120.83 (C-3”), 116.20 (C-3” and C-5”), 116.62 (C-4’).

(E)-3-(4-chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one (24)

MS: M⁺ at m/z 232.5. Anal. Calcd for C₁₃H₉ClO₂: C, 67.11; H, 3.90%. Found: C, 67.28; H, 3.88%. ¹H NMR (200 MHz, CD₃OD): δ 6.63 (m, 1H, H-4”), 7.28 (m, 5H, H-2”, 3”, 5”, 6” and 3”), 7.43 (d, 1H, J = 15.78 Hz, H-2), 7.72 (d, 1H, J = 1.64 Hz, H-5”), 7.79 (d, 1H, J = 15.78 Hz, H-3). ¹³C NMR (100 MHz, CD₃OD): δ 177.86 (C-1), 152.91 (C-2’), 148.53 (C-5’), 144.65 (C-3), 134.34 (C-4’), 134.02 (C-1”) 129.18 (C-2” and C-6”), 130.67 (C-3” and 5”), 120.89 (C-2’), 111.92 (C-4”).

(E)-3-(4-Dimethylaminophenyl)-1-(furan-2-yl)prop-2-en-1-one (25)

MS: M⁺ at m/z 241. Anal. Calcd for C₁₃H₁₅NO₂: C, 67.11; H, 3.90%. Found: C, 67.18; H, 3.85%. ¹H NMR (400 MHz,
DMSO-d$_6$): δ 3.43 (s, 6H, N(CH$_3$)$_2$), 6.72 (m, 1H, H-4’), 6.78 (d, 2H, J = 8.02 Hz, H-3” and H-5”), 7.40 (d, 1H, J = 15.07 Hz, H-2), 7.63 (d, 1H, J = 2.01 Hz, H-3’), 7.65 (d, 1H, J = 15.07 Hz, H-3), 7.67 (d, 2H, J = 8.02 Hz, H-2” and H-6”), 7.94 (m, 1H, H-5’). 13C NMR (100 MHz, DMSO-d$_6$): δ 177.18 (C-1), 153.90 (C-2’), 152.49 (C-5”), 147.96 (C-4”), 144.36 (C-3), 131.13 (C-2” and C-6”), 122.18 (C-1”), 118.36 (C-2), 116.41 (C-3”), 112.99 (C-4”), 112.22 (C-3” and C-5”), 40.38 (CH$_3$)$_2$.

(E)-3-(3-Nitrophenyl)-1-(furan-2-yl)-prop-2-en-1-one (26)

MS: M$^+$ at m/z 211. Anal. Calcd for C$_{13}$H$_9$NO$_2$: C, 64.20; H, 3.73; N, 5.76 %. Found: C, 64.28; H, 3.75; N, 5.86 %. 1H NMR (400 MHz, DMSO-d$_6$): δ 6.80 (bs, 1H, H-4’), 6.98 (d, 1H, J = 15.82 Hz, H-2), 7.74 (m, 1H, H-3”), 7.57 (m, 1H, H-5”), 7.78 (m, 3H, H-3, H-6”, H-5”), 8.26 (m, 2H, H-4” and H-2”). 13C NMR (100 MHz, DMSO-d$_6$): δ 176.2 (C-1), 152.71 (C-2’), 148.77 (C-3’), 148.36 (C-3”), 140.32 (C-3), 136.28 (C-1”), 134.89 (C-6”), 130.31 (C-5”), 124.62 (C-2 and C-2”), 122.86 (C-3”), 120.37 (C-4”), 112.75 (C-4’).

(E)-3-(Phenyl)-1-(furan-2-yl)-prop-2-en-1-one (27)

MS: M$^+$ at m/2 198. Anal. Calcd for C$_{13}$H$_{10}$O$_2$: C, 78.77; H, 5.09 %. Found: C, 78.81; H, 5.11 %. 1H NMR (400 MHz, CDCl$_3$): δ 6.62 (m, 1H, H-4’), 7.38 (dd, 1H, J = 1.4 Hz and 3.2 Hz, H-3”), 7.45 (d, 1H, J = 2.0 Hz, H-5”), 7.47 (m, 2H, H-3”, H-5”), 7.48 (d, 1H, J = 16.02 Hz, H-2), 7.68 (m, 3H, H-4”, H-2” and 6”), 7.92 (d, 1H, J = 16.02 Hz, H-3”). 13C NMR (100 MHz, CDCl$_3$): δ 178.00 (C-1), 153.71 (C-2’), 146.54 (C-4”), 143.97 (C-3), 134.73 (C-1”), 130.61 (C-4”), 128.95 (C-3” and C-5”), 128.53 (C-2” and C-6”), 121.18 (C-2), 117.52 (C-3”), 112.55 (C-4’).

(E)-3-(2-Chloro-5-nitrophenyl)-1-(furan-2-yl)-prop-2-en-1-one (28)

MS: M$^+$ at m/2 277.5. Anal. Calcd for C$_{13}$H$_8$ClNO$_2$: C, 56.23; H, 2.90; N, 5.04%. Found: C, 56.37; H, 2.95; N, 5.14%. 1H NMR (500 MHz, CDCl$_3$): δ 6.66 (m, 1H, H-4’), 7.45 (d, 1H, J = 3.5 Hz, H-3”), 7.58 (d, 1H, J = 15.02 Hz, H-2), 7.65 (d, 1H, J = 8.32 Hz, H-3”), 7.73 (d, 1H, J = 1.24 Hz, H-5”), 8.17 (m, 1H, H-4”), 8.21 (d, 1H, J = 15.7 Hz, H-3), 8.63 (d, J = 2.62 Hz, 1H, H-6”). 13C NMR (125 MHz, CDCl$_3$): δ 176.97 (C-1), 153.22 (C-2’), 147.39 (C-
5'), 146.78 (C-5”), 141.89 (C-3), 137.26 (C-2”), 134.62 (C-1”), 132.40 (C-3”), 126.13 (C-6”), 125.20 (C-4”), 122.58 (C-3’), 118.83 (C-2), 113.30 (C-4’).

(E)-3-(2, 3-Dimethoxy-phenyl)-1-(furan-2-yl)prop-2-en-1-one (29)

MS: M⁺ at m/z 258. Anal. Calcd for C₁₅H₁₄O₄: C, 69.76; H, 5.46%. Found: C, 69.98; H, 6.60%. ¹H NMR (400 MHz, CDCl₃): δ 3.81 (s, 6H, 2×-OCH₃), 6.61 (m, 1H, H-4’), 7.00 (m, 1H, H-5”), 7.21 (d, 1H, J= 8.00 Hz, H-6”), 12.79 (d, 1H, J = 3.5 Hz, H-3’), 7.42 (d, 1H, J = 15.67 Hz, H-2), 7.65 (d, 1H, J = 8.00 Hz, H-4”), 7.73 (d, 1H, J = 1.23 Hz, H-5’), 8.21 (d, 1H, J = 15.67 Hz, H-3). ¹³C NMR (100 MHz, CDCl₃): δ 176.19 (C-1), 153.22 (C-2’), 148.56 (C-5’), 147.39 (C-3”), 145.05 (C-2”), 141.45 (C-3), 122.85 (C-5”), 121.58 (C-2), 120.66 (C-6”), 122.02 (C-3’), 118.84 (C-1”), 113.30 (C-4”), 55.96 (2”-OCH₃), 55.34 (3”-OCH₃).

(E)-3-(Benzo[d][1,3]dioxol-6-yl)-1-(furan-2-yl)prop-2-en-1-one (30)

MS: M⁺ at m/z 242. Anal. Calcd for C₁₄H₁₀O₄: C, 69.42; H, 4.16%. Found: C, 69.65; H, 4.26%. ¹H NMR (400 MHz, CDCl₃): δ 6.03 (s, 2H, -OCH₂O), 6.70 (dd, 1H, J = 1.62 and 3.55 Hz, H-4’), 6.88 (d, 1H, J = 8.05 Hz, H-5’), 7.19 (d, 1H, J = 1.46 Hz, H-6”), 7.34 (bs, 1H, H-6”), 7.45 (d, 1H, J = 15.61 Hz, H-2), 7.56 (d, 1H, J = 3.55 Hz, H-3”), 7.76 (d, 1H, J = 15.61 Hz, H-3”), 7.85 (d, 1H, J = 1.62 Hz, H-5’). ¹³C NMR (100 MHz, CDCl₃): δ 177.29 (C-1), 153.29 (C-2’), 149.82 (C-5’), 149.25 (C-3”), 148.73 (C-4”), 140.52 (C-3), 122.85 (C-5”), 121.82 (C-3’), 120.25 (C-6”), 116.92 (C-1”), 113.26 (C-2”), 112.83 (C-4’), 102.54 (OCH₂O-).

(E)-3-(3,4-Dimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one (31)

MS: M⁺ at m/z 258. Anal. Calcd for C₁₅H₁₄O₄: C, 69.76; H, 5.46%. Found: C, 69.88; H, 6.51%. ¹H NMR (500 MHz, CDCl₃): δ 3.89 (s, 3H, -OCH₃), 3.92 (s, 3H, -OCH₃), 6.71 (dd, 1H, J = 1.65 & 3.51 Hz, H-4’), 7.02 (d, 1H, J = 8.24 Hz, H-5’), 7.46 (m, 4H, H-3’, H-2”, H-6” & H-2), 7.81 (d, 1H, J = 14.60 Hz, H-3), 7.85 (bs, 1H, H-5’). ¹³C NMR (125 MHz, CDCl₃): 178.43 (C-1), 154.196 (C-2’), 151.86 (C-5’), 149.57 (C-3”), 148.67
(C-4”), 144.49 (C-3), 128.07 (C-1”), 123.76 (C-2), 119.34 (C-3’), 117.55 (C-6”), 112.88 (C-5”), 114.4 (C-4’), 110.42 (C-2”), 56.36 (OCH$_3$)$_2$.

(E)-3-(4-Nitrophenyl)-1-(furan-2-yl)prop-2-en-1-one (32)

MS: M$^+$ at m/z 243 Anal. Calcd for C$_{13}$H$_9$NO$_4$: C, 64.20; H, 3.74; N, 5.76 %. Found: C, 64.31; H, 3.78; N, 5.87 %. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 6.83 (m, 1H, H-4’), 7.82 (d, 1H, J = 15.18 Hz, H-2), 7.90 (d, 1H, J = 3.8 Hz, H-3’), 8.11 (d, 1H, J = 1.6 Hz, H-5’), 8.14 (d, 2H, J = 8.8 Hz, H-2” & H-6”), 8.20 (d, 1H, J = 15.18 Hz, H-3), 8.29 (d, 2H, J = 8.8 Hz, H-3” and H-5”). $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta$ 176.14 (C-1), 152.7 (C-2’), 148.94 (C-5’), 148.08 (C-4”), 140.88 (C-3), 139.99 (C-1”), 129.76 (C-2” and C-6”), 125.89 (C-2), 123.93 (C-3” and C-5”), 120.51 (C-3’), 112.87 (C-4”).

(E)-3-(4-Bromophenyl)-1-(furan-2-yl)prop-2-en-1-one (33)

MS: M$^+$ at m/z 277 Anal. Calcd for C$_{13}$H$_9$BrO$_2$: C, 56.34, 3.27; H, 5.46 %. Found: C, 56.49, H, 3.29%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.60 (m, 1H, H-4’), 7.35 (dd, 1H, J = 1.6 & 3.2 Hz, H-3’), 7.44 (d, 1H, J = 16 Hz, H-2), 7.5 (dd, 2H, J = 8.02 Hz and 1.63 Hz, H-2” and H-6”), 7.66 (m, 1H, H-5’), 7.72 (dd, 2H, J = 8.02 Hz and 1.63 Hz, H-3” and H-5”), 7.84 (d, 1H, J = 16 Hz, H-3). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 177.73 (C-1), 153.62 (C-2’), 146.63 (C-5’), 142.53 (C-3), 133.66 (C-1”), 132.21 (C-3” and 5”), 129.87 (C-2” and 6”), 124.89 (C-4”), 121.71 (C-2), 117.68 (C-3’), 112.66 (C-4”).

(E)-3-(4-Methoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one (34)

MS: M$^+$ at m/z 228 Anal. Calcd for C$_{14}$H$_{12}$O$_3$: C, 73.67; H, 5.30%. Found: C, 73.81; H, 5.34%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.83 (s, 3H, -OCH$_3$), 6.58 (dd, J = 1.68, 2.01 Hz, 1H, H-4’), 6.92 (m, 2H, H-3” and H-5”), 7.30 (d, 1H, J = 4.4 Hz, H-3”), 7.32 (d, 1H, J = 16.0 Hz, H-2), 7.60 (m, 2H, H-2” and H-6”), 7.63 (m, 1H, H-5’), 7.84 (d, 1H, J = 16 Hz, H-3). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 178.16 (C-1), 161.76 (C-4”), 153.86 (C-2’), 146.32 (C-5’), 143.82
(C-3), 130.34 (C-2" and C-6"), 127.48 (C-1''), 118.85 (C-2), 117.35 (C-3''), 114.43 (C-3" and C-5''), 112.4 (C-4''), 55.41 (OCH₃).

(E)-3-(3, 4, 5-Trimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one (35)

MS: M⁺ at m/z 288. Anal. Calcd for C₁₆H₁₆O₅: C, 66.66; H, 5.59 %. Found: C, 69.76; H, 5.56 %. ¹H NMR (200 MHz, CDCl₃): δ 3.81 (s, 3H, -OCH₃), 3.91 (s, 6H, 2x -OCH₃), 6.71 (dd, 1H, J = 1.63 and 3.58 Hz, H-4'), 7.08 (s, 2H, H-2" & 6''), 7.55 (d, 1H, J = 15.67 Hz, H-2), 7.63 (d, 1H, J = 3.58 Hz, H-3''), 7.78 (d, 1H, J = 15.67 Hz, H-3), 7.87 (bs, 1H, H-5''). ¹³C NMR (100 MHz, CDCl₃): δ 177.82 (C-1), 162.34 (C-3" and C-5''), 153.63 (C-2''), 149.38 (C-5''), 140.59 (C-3), 140.13 (C-4''), 129.56 (C-1''), 122.56 (C-2), 121.89 (C-3''), 113.23 (C-4''), 110.6 (C-2" and C-6''), 56.52(OCH₃), 56.23 (OCH₃)₂.

(E)-3-(2, 5-Dimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one (36)

MS: M⁺ at m/z 258. Anal. Calcd for C₁₅H₁₄O₄: C, 69.76; H, 5.46 %. Found: C, 69.88; H, 5.51 %. ¹H NMR (200 MHz, CDCl₃): δ 3.88 (s, 6H, 2x -OCH₃), 6.72 (dd, 1H, J = 1.58 & 3.61 Hz, H-4'), 7.13 (m, 2H, H-3" & H-4''), 7.43 (m, 1H, H-6''), 7.56 (bs, 1H, H-3''), 7.62 (d, 1H, J = 15.93 Hz, H-2), 7.88 (bs, 1H, H-5''), 8.16 (d, 1H, J = 15.93 Hz, H-3). ¹³C NMR (100 MHz, CDCl₃): δ 177.45 (C-1), 162.43 (C-5''), 162.03 (C-2''), 153.23 (C-2''), 149.82 (C-5''), 140.25 (C-3), 121.46 (C-2), 121.35 (C-3''), 116.25 (C-1''), 115.26 (C-3''), 115.03 (C-4''), 112.39 (C-4''), 111.37 (C-6''), 55.93 (OCH₃), 55.23 (OCH₃).

7.3. X-Ray studies

The crystal of compound 9 used for data collection was of dimension 0.3 x 0.2 x 0.1 mm. X-ray intensity data of 6806 reflections (of which 2673 unique) were collected. The cell dimensions were determined by least-square fit of angular settings of 2440 reflections in the θ range 2.59 to 27.45°. The structure was solved by direct methods using SHELXS 97 (Hijova and Listy 2006). All the hydrogen atoms were located on a difference electron density map and their positional and isotropic thermal parameters were included in the refinement. The final refinement cycles converged to an R = 0.0343 and wR (F²) = 0.0879 for the observed data 0.59. The
crystallographic data are summarized in Table 3. CCDC - 776070 contains the supplementary crystallographic data for this molecule.

8. BIOEVALUATION

8.1. In vitro combination (EPI) study of ciprofloxacin in combination with compounds.

The ciprofloxacin/compounds combination studies were performed on *S. aureus* 1199B in Mueller Hinton broth (Difco). The MIC of ciprofloxacin was determined in the presence of increasing concentrations of compounds by broth checkerboard method in micro titre plates (Lawrence *et.al.*, 2006). The 2-fold serial dilutions of ciprofloxacin ranging from 0.03 to 16 µg/mL, were tested in combination with compounds at seven different concentrations (0.78-50 µg/mL). The final bacterial inoculum of $5 \times 10^5$ cfu/mL was added to each well. The plates were incubated for 18 h at 37°C and the wells were assessed visually for growth. The minimum concentration of compounds that produced the maximal reduction in the MIC of ciprofloxacin was determined. The minimal effective concentration (MEC) was determined to be the minimal concentration of EPI that produced the maximal reduction in substrate MIC. No further decrease in substrate MIC was observed at EPI concentrations greater than the MEC (Sheldrick, 1997).

8.2. Anti-cancer activity

*Cell culture, growth conditions and treatment*

All the cancer cell lines (HL-60, MOLT-4, PC-3 and HeLa) were obtained from National Cancer Institute (NCI), Bethesda, USA. The cells were grown in RPMI-1640 medium supplemented with 10% heat inactivated fetal bovine serum (FBS), penicillin (100 units/mL), streptomycin (100 µg/mL), L-glutamine (0.3 mg/mL), pyruvic acid (0.11 mg/mL), and 0.37% NaHCO$_3$. Cells were grown in CO$_2$ incubator (Thermocon Electron Corporation, USA) at 37°C in an atmosphere of 95% air and 5% CO$_2$ with 98% humidity. Compounds (1-36) were dissolved in DMSO and delivered to cell culture in a complete medium.

*Cell proliferation assay*

HL-60 and MOLT-4 cells were plated in 96 well plates at the density of 15000 cells per well/200µl of the medium. Adherent cells (PC-3 and HeLa) were treated when they were 75% confluent in 96 well plates. Cultures were treated with four different concentrations (1µm, 10 µm, 30 µm and 100 µm) of compounds (1-36) for 48 hours to determine IC$_{50}$ values. 20µL of MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide) of concentration
(2.5mg/mL) was added to each well and incubated at 37º C for three hours. The plates were centrifuged at 2000 rpm for 15 minutes, and supernatant were discarded and the MTT formazan crystals were dissolved in 150μL of DMSO. Plates were shaken on a shaker for 3 minutes and then incubated at 37ºC for five minutes. The OD measured at 570 nm.

8.3. Anti inflammatory activity

Animal

Wistar rats (12-16 week old, weighing between 130-150 mg) were housed in polycarbonate cages in the animal house. They were fed with pellet diet and water ad libitum during the course of experimentation. Light cycle was automatically controlled for 12 h. Light and dark cycle (on at 7.00 AM and off at 7.00 PM). Room temperature was regulated at 26±1ºC. Animals were housed in such conditions for 3-4 days prior to the experimentation for acclimatization.

Preparation of test material

The test material was prepared freshly as fine homogenized suspension in 2% gum acacia (w/v) for administration.

Carrageenan induced inflammation Assay

Edema was induced in groups of four rats by injecting 100 μL of 1% (w/v) freshly prepared carrageenan solution in normal saline into the sub planter region of the left hind paw while the right paw received an equal volume of normal saline. Test compounds were administered orally 45 min. before carrageenan injection at 100mg/kg. Volume of the paw was measured immediately and 4 h after carrageenan injection with a volume differential meter model 7101, Ugo Basile (Italy). Percent inhibition of the test compound was calculated.

Statistical Evaluation

The numerical values were expressed as Mean ± SEM of difference between vehicle control and treatment groups, unless otherwise specified.

8.4. In vitro antioxidant activity (DPPH method)

Test solution was prepared by dissolving DPPH solution 45 μg/mL in methanol while samples were prepared in D.W. (distilled water)/methanol/PBS. Standard Ascorbic acid was prepared (Ascorbic acid 10 mg/mL or 1mg/mL stock solution dissolved in distilled water). The free-radical scavenging activity of EPA was measured in terms of hydrogen donating or radical-
scavenging ability using the stable radical 1,1-diphenyl-2-picrylhydrazyl (DPPH). A 1mM solution of DPPH in ethanol was used. For the assay, the reaction mixture contains 10 µL of test drug in 990 µL of DPPH solution in 48 well microtiter plates and incubated at room temperature for 30 min (Lee and Chung). Absorbance was measured at 517 nm in ELISA reader (Thermo multiscan spectrum). The capacity to scavenge DPPH radical was calculated (Eliopoulos et al., 1996). DPPH was dissolved in methanol and sonicated for 5 min to obtain the stable free radical DPPH•. The test compounds were diluted in different concentrations with the DPPH• solution in a 48-well microplate. Ascorbic acid was used as control in each series. The compounds 1-36 were tested in triplicate at different concentration, such that a 50% fall in absorbance of the DPPH• can be calculated. The absorbance of the reaction mixture was measured after 20 min incubation at room temperature using a microplate ELISA reader at 517 nm. The IC50 of each sample was determined and compared with standard ascorbic acid.

9. Molecular modeling

The coordinates of tubulin complexed with colchicine were obtained from a protein data bank (PDB entry: 1SA0). The structure of compound 25 was drawn in MOE and subjected to energy minimization using MMFF94x force field. The ligands were docked at the colchicine-binding site of tubulin using the GOLD 4.0.1. Gold performs genetic algorithm based ligand docking to optimize the conformation of ligand at the receptor binding site. It utilizes GOLD score fitness function to evaluate the various conformations of ligand at the binding site and comprises four components: protein-ligand hydrogen bond energy, protein-ligand vander Waals (vdw) energy, ligand internal energy, and ligand torsional strain energy.
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