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Design and Synthesis of Novel pyrazol-1-carboxamide analogues as potent antioxidant agents

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5.1 Abstract:

A series of novel pyrazol-1-carboxamide derivatives **5(a-g)** was efficiently synthesized through a straightforward cycloaddition reaction between various substituted chalcones and semicarbazide under acidic conditions. The structures of all synthesized compounds were confirmed using spectroscopic techniques like IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectrometry. The antioxidant activity was assessed using multiple in vitro assays, by DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging methods. certain compounds **5C**, and **5g** shows excellent activity toward radical scavenging activity.

Keywords: chalcones, antioxidant activity and DPPH,

5.2 Introduction:

Pyrazol-1-yl carboxamides constitute a prominent class of heterocyclic compounds whose unique structural motif—a carboxamide group directly linked to the nitrogen at the 1-position of a pyrazole ring—has established them as a privileged scaffold in modern drug discovery [1]. The pyrazole core itself is a diazole, a five-membered aromatic ring featuring two adjacent nitrogen atoms, which contributes to the molecule, stability and ability to engage in diverse non-covalent interactions with biological targets. The incorporation of the carboxamide group significantly enhances this potential by introducing a key pharmacophore capable of acting as both a hydrogen bond donor and acceptor. This combination allows pyrazol-1-ylcarboxamides to effectively mimic peptide bonds and integrate into enzyme active sites or receptor pockets, making them highly effective for modulating a wide array of physiological pathways [2]. The synthetic flexibility to introduce a vast range of substituents on the

pyrazole ring and the amide nitrogen allows for precise fine- tuning of their electronic, steric, and physicochemical properties, which is crucial for optimizing drug-like characteristics such as solubility, metabolic stability, and membrane permeability [3]. The medicinal significance of pyrazol-1-yl carboxamides is demonstrated by their broad and potent pharmacological profile, leading to applications across multiple therapeutic domains. In oncology, this scaffold is a cornerstone of targeted therapy, most notably exemplified by drugs like Crizotinib, an ALK and ROS1 inhibitor used to treat non-small cell lung cancer [4]. The pyrazol-1-yl carboxamide moiety in such agents is critical for achieving high-affinity binding to kinase domains. Beyond oncology, derivatives have been developed as potent anti-inflammatory agents by inhibiting enzymes like cyclooxygenase-2 (COX-2) and cytokines involved in the inflammatory cascade [5]. Furthermore, this chemical class has yielded numerous compounds with significant antimicrobial activity, demonstrating efficacy against a spectrum of drug-resistant bacterial and fungal pathogens [6]. The versatility also extends to central nervous system disorders, with research exploring its utility in developing anticonvulsant and antidepressant agents, underscoring its capacity to cross the blood-brain barrier and interact with neurological targets [7]. A particularly compelling and extensively researched area of their bioactivity is their potent antioxidant potential. Oxidative stress, characterized by an overproduction of reactive oxygen species (ROS), is a key pathological contributor to aging, neurodegenerative diseases like Alzheimer, Parkinson, diabetes, and cardiovascular disorders. Pyrazol-1-yl carboxamide derivatives have been strategically designed to counteract this damage [8]. Their antioxidant mechanism is often multifunctional; the scaffold can directly scavenge free radicals like DPPH, ABTS, and hydroxyl radicals, thereby neutralizing their damaging effects on cellular components such as lipids, proteins, and DNA [9]. The activity is highly dependent on the nature of the substituents. Electron-donating groups (e.g., -OH, -OCH3) attached to the phenyl rings of the carboxamide or the pyrazole core significantly enhance radical scavenging ability by stabilizing the resulting phenoxyl radicals [10]. Some derivatives also function as metal chelators, sequestering transition metal ions like Fe^{2+} and Cu^{2+} that catalyze the Fenton reaction, a major source of highly destructive hydroxyl radicals [11]. The synthesis of pyrazol-1-yl carboxamides primarily revolves around the formation of the critical amide bond, with the most common and efficient strategies involving the coupling of a pre-formed 1H-pyrazole carboxylic acid with various amines [12]. The first step typically involves the preparation of the carboxylic acid precursor, which can be achieved through classical cyclization reactions such as the Knorr pyrazole synthesis between hydrazines and 1,3-dicarbonyl compounds [13], or via more modern methodologies employing click chemistry or cycloaddition reactions [14]. Once the pyrazole-1-carboxylic acid

is in hand, the direct coupling approach using activating agents is widely employed. Reagents such as carbodiimides (EDC, DCC), phosphonium salts (PyBOP), or uranium salts (HATU) are used to activate the carboxylic acid, forming a reactive intermediate like an O-acylisourea or an active ester, which is then attacked by the nucleophilic amine to yield the target carboxamide [15]. This one-pot method is highly favored in medicinal chemistry for its operational simplicity, high yields, and excellent functional group tolerance, especially when performed in the presence of additives like HOBt or HOAt to prevent racemization and facilitate the coupling process [16]. An alternative and highly effective two-step pathway involves the conversion of the pyrazole-1-carboxylic acid into its corresponding acid chloride as a key intermediate. This transformation is typically accomplished by treating the acid with highly reactive chlorinating agents such as thionyl chloride ($SOCl_2$) or oxalyl chloride [$(COCl)_2$] [17]. The resulting acid chloride, being highly electrophilic, readily undergoes nucleophilic acyl substitution with a wide range of amines under mild basic conditions, often using a base like triethylamine or pyridine to neutralize the hydrochloric acid generated during the reaction [18]. While this method is exceptionally powerful and gives high conversion rates, its main drawback is the potential incompatibility with acid- or base-labile functional groups on either the pyrazole or the amine reactant [19]. The choice between the direct coupling method and the acid chloride route is ultimately dictated by the scale, the stability of the starting materials, and the need for atom economy, with the former generally being preferred for complex and sensitive molecules in modern drug discovery pipelines [20].

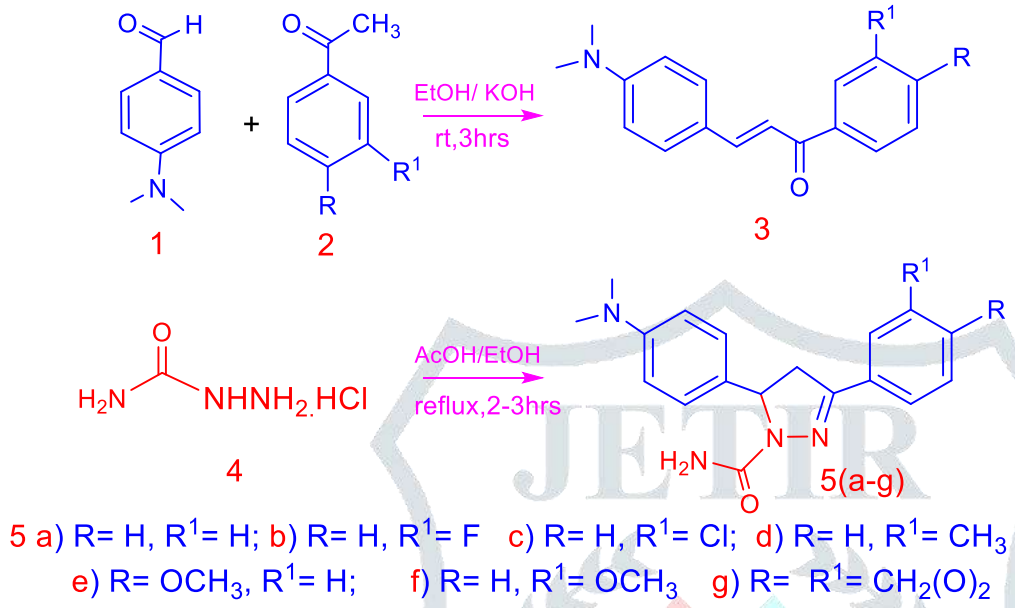
5.3 Materials andmethods:

The reagents and solvents were commercially purchased from Sigma Aldrich and used without further purification. The progress of the reactions was monitored by TLC using E. Merck silica gel GF254 precoated on aluminum-backed plates. Visualization of the developed chromatograms was performed using UV light (254 and 356 nm). Melting point ranges of solid compounds were determined in an open capillary tube and are uncorrected. IR spectra were recorded in a KBr matrix using a Perkin-Elmer spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded using a agilent 400 and 100 MHz spectrometer with Chloroform as the solvent.

5.4 Plan of the synthesis

Initially, the required intermediates 3-(4-(dimethylamino)aryl)-1-phenylprop-2-en-1-ones, **3(a-g)** were synthesized by base catalyzed Claisen-Schmidt reaction of 4-(dimethylamino)benzaldehyde **1** with substituted

acetophenones, **2**(**a-g**), in ethyl alcohol. Then, the cyclocondensation reaction of chalcones, **3**(**a-g**) with semicarbazide hydrochloride, **4** in acidic medium under reflux conditions produced pyrazole carbothioamide derivatives **5**(**a-g**) in good yields. The schematic representation for the synthesis of **5(a-g)** was depicted in **Figure 5.1**.



Scheme 5.1: Schematic diagram for the synthesis of pyrazole carbothioamides, **5**(**a-g**)

5.5 Discussion on the experiments leading to the synthesis of 5-(4-(dimethylamino)phenyl)-3-(aryl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5(a-g)

we considered 5-(4-(dimethylamino)phenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, **5d** as a repsresentive compound the synthetic route is illustrated in **fig 1**

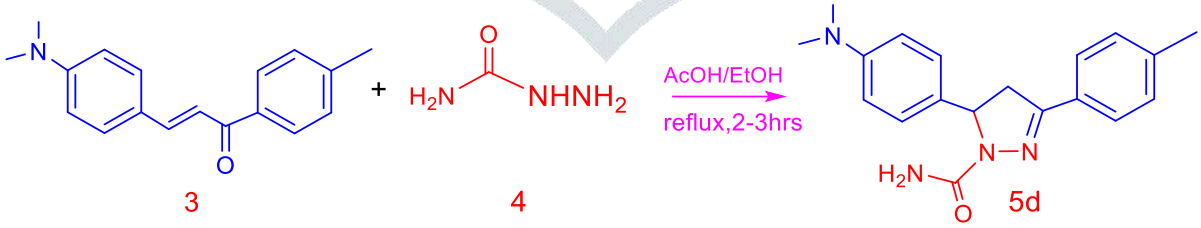


Figure 1. Reaction pathway for the synthesis of the pyrazolecarboxamide derivatives.

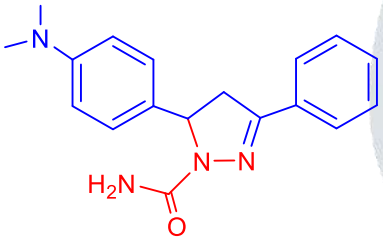
5-(4-(dimethylamino)phenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazole-1-carboxamide (5d) : Obtained from (*E*)-3-(4-(dimethylamino)phenyl)-1-(p-tolyl)prop-2-en-1-one, **1** (2.65 gm, 10 mmole) and semicarbazide, **2** (1.1 gm, 10 mmole) in 72% yield (3.01 g) m.p., 142-144˚C.

In ^{1}H NMR studies reveals the formation of pyrazolines the compound 5d whch shows the=ree doublet of doublet in the ranges 3.117-3.168 (dd, 1H, C_4-H_a, *j*=2.8, 17.6Hz), 3.659-3.730 (dd, 1H, C_4-H_b, *j*=3.1, 16.0 Hz), 5.409-5.446 (dd, 1H, C_5-H_c, *j*=3.2, 11.6 Hz) the splitting is due to three diastereomeric protons. The two methyl groups attached to amine show singlet peak at δ 2.887 ppm the methyl group shows a singlet peak at 2.372 ppm. The broad peak for amide proton appears at δ 5.221 ppm. The aromatic protons shown an array of signals in the range of δ 6.656 - 7.583 ppm. The elemental analysis satisfied with the obtained result.

5.5.1 General procedure for the synthesis of 5-aryl-3-(5-chlorothiophen-2-yl)-4,5-dihydro-1*H*-pyrazole-carbothioamides, 5(a-g)

A solution mixture of chalcones, **5**(**a-g**) (10 mmol) and semicarbazide hydrochloride, **4** (10 mmol) in acetic acid (40%) was refluxed on a water bath for 3-4 h. The progress of the reaction was monitored by TLC. After the completion, the mixture was filtered and the filtrate was poured into crushed ice. The separated solids were filtered and washed successively with 5% $NaHCO_3$ and water. The crude solids were recrystallized from methyl alcohol to get target molecules **5**(**a-g**) in good yields.

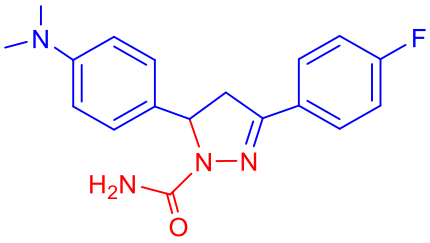
5.5.2 5-(4-(dimethylamino)phenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide, 5a



Obtained from 3-(4-(dimethylamino)phenyl)-1-phenylprop-2-en-1-one, **3a** (2.51g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 75% yield, m.p. 158-161 °C.

IR (KBr) ν_{max} (cm^{-1}): 3252 (NH), 2956 (CH), 1555 (C=N), 1248 (C=S), 1020 (C–N), 720 (C-Cl). ^{1}H NMR ($CDCl_3$, δ ppm): 3.02 (s, 6H, $2CH_3$), 3.05-3.11 (dd, 1H, *J=3.2, 17.6Hz*, C_4-H_a), 3.73-3.81 (dd, 1H, *J=12.0, 17.6Hz*, C_4-H_b), 5.97-6.01 (dd, 1H, *J=3.6, 11.2Hz*, C_5-H), 6.22 (s, 2H, NH_2), 6.87-7.06 (m, 5H, Ar-H), 7.15-7.29 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.30 (2C, CH_3), 41.68 (1C, C-4), 69.56 (1C, C-5), 124.40 (1C), 125.35 (1C), 125.90 (1C), 126.62 (2C), 127.36 (1C), 128.10 (2C), 130.20 (2C), 140.54 (2C), 153.50 (1C, C-3), 155.10 (1C, C=O). MS *m/z*: 308.16 (M+, 100); Anal. Calcd. for $C_{18}H_{20}N_4$ (%): C, 70.11; H, 6.54; N, 18.17; Found: C, 70.05; H, 6.49; N, 18.11.

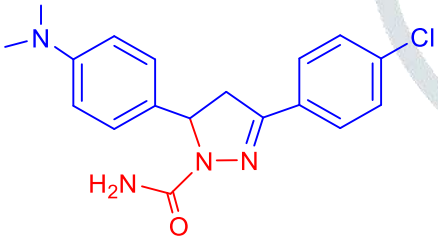
5.5.3 5-(4-(dimethylamino)phenyl)-3-(4-fluorophenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5b



Obtained from 3-(4-(dimethylamino)phenyl)-1-(p-fluoro)prop-2-en-1-one, **3b** (2.65g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 72 % yield, m.p. 165-168 °C.

IR (KBr) ν_{max} (cm^{-1}): 3258 (NH), 2959 (CH), 1570 (C=N), 1251 (C=O), 1027 (C–N). ^{1}H NMR ($CDCl_3$, δ ppm): 3.02 (s, 6H, $2CH_3$), 3.61-3.77 (dd, 1H, *J=3.8, 16.0Hz*, C_4-H_a), 3.92-4.01 (dd, 1H, *J=12.1, 17.1Hz*, C_4-H_b), 5.99-6.05 (dd, 1H, *J=3.9, 12.2Hz*, C_5-H), 6.21 (s, 2H, NH_2), 6.88-7.16 (m, 4H, Ar-H), 7.160-7.238 (m, 2H, Ar-H), 7.55-7.66 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.3(2C, CH_3), 40.94 (1C, C-4), 67.82 (1C, C-5), 116.60 (2C), 125.30 (1C), 125.90 (1C), 127.85 (1C), 129.05 (2C), 130.40 (2C), 135.46 (1C), 153.44 (1C, C-3), 159.51 (1C), 155.36(1C, C=O), 165.2 (1C). MS (*m/z*): 326.14 (M+, 100), 327.15 (M+, 19); Anal. Calcd. for $C_{18}H_{19}FN_4O$ (%): C, 66.24; H, 5.87; N, 17.17; Found: C, 66.16; H, 5.79; N, 17.12.

5.5.4 3-(4-chlorophenyl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5c

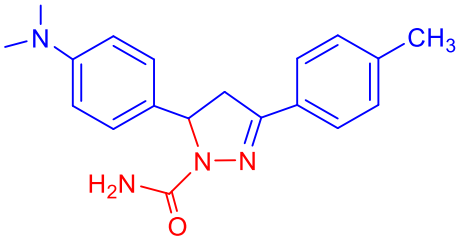


Obtained from 1-(4-chlorophenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one, **3c** (2.85g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 80% yield, m.p. 165-167 °C.

IR (KBr) ν_{max} (cm^{-1}): 3255 (NH), 2950 (CH), 1569 (C=N), 1647 (C=o), 1023 (C–N). ^{1}H NMR ($CDCl_3$, δ ppm): 3.05 (s, 6H, $2CH_3$) 3.051-3.105 (dd, 1H, *J=3.6, 17.0Hz*, C_4-H_a), 3.720-3.800 (dd, 1H, *J=11.9, 17.0Hz*, C_4-H_b), 5.990-6.030 (dd, 1H, *J=3.8, 11.0Hz*, C_5-H), 6.24 (s, 2H, NH_2), 6.909-7.080 (m, 4H, Ar-H), 7.190-7.275 (m, 2H, Ar-H), 7.62-7.67 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.3 (2C, CH_3) 40.44 (1C, C-4), 67.90 (1C, C-5), 112.72 (2C), 125.80 (1C), 126.95 (2C), 128.10 (1C), 130.42 (1C), 131.26 (1C), 131.90 (1C), 132.46 (1C), 136.6 (1C) 137.94 (1C), 153.44 (1C, C-3), 183.35 (1C, C=O). MS (*m/z*):

342.12 (M+, 100), 344.12 (M+, 33); Anal. Calcd. for $C_{18}H_{19}ClN_3O$ (%): C, 63.06; H, 5.59; N, 16.34; Found: C, 63.0; H, 5.51; N, 16.27.

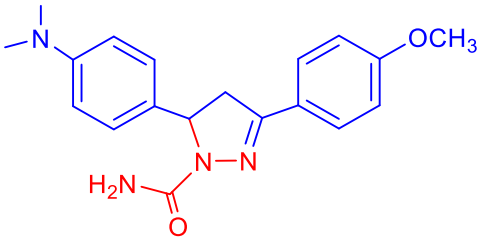
5.5.5 5-(4-(dimethylamino)phenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5d



Obtained from 3-(4-(dimethylamino)phenyl)-1-(p-tolyl)prop-2-en-1-one, **1** (2.65 gm, 10 mmole) and semicarbazide, **2** (1.11 gm, 10 mmole) in 72% yield (3.01 g) m.p., 142-144˚C.

IR (KBr) ν_{max} (cm^{-1}): 3265 (NH), 2970 (CH), 1565 (C=N), 1270 (C=S), 1040 (C–N); ^{1}H NMR ($CDCl_3$; δ ppm): 2.372 (s, 3H, CH_3), 2.887 (s, 6H, CH_3), 3.117-3.168 (dd, 1H, C_4-H_a, *j*=2.8, 17.6Hz), 3.659-3.730 (dd, 1H, C_4-H_b, *j*=3.1, 16.0 Hz), 5.221 (s, 2H, NH_2), 5.409-5.446 (dd, 1H, C_5-H_c, *j*=3.2, 11.6 Hz), 6.656-6.672 (d, 2H, Ar-H), 7.116-7.133 (d, 2H Ar-H), 7.186-7.204 (d, 2H Ar-H), 7.566-7.583 (d, 2H Ar-H); ^{13}CNMR ($CDCl_3$; δ ppm): 21.418 (1C, CH_3), 40.613 (2C, CH_3), 42.861 (1C, C-4), 59.605 (1C, C-5), 112.852 (2C, Ar-C), 126.327 (2C, Ar-C), 126.473 (2C, Ar-C), 128.876 (2C, Ar-C), 129.343 (1C, Ar-C), 130.559 (1C, Ar-C), 140.142 (1C, Ar-C), 150.095 (1C, Ar-C), 151.895 (1C, C-3), 155.232 (1C, C=O). MS (*m/z*): 322.18 (M+); Anal. Calcd. for $C_{19}H_{22}N_4O$ (%): C, 70.78; H, 6.88; N, 17.38; Found: C, 70.72; H, 6.81; N, 17.34.

5.5.6 5-(4-(dimethylamino)phenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5e

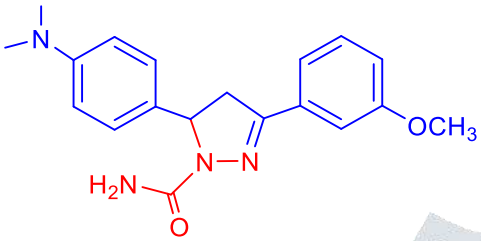


Obtained from 3-(4-(dimethylamino)phenyl)-1-(4-methoxyphenyl)prop-2-en-1-one, **3e** (2.81g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 75% yield, m.p. 168-170 °C.

IR (KBr) ν_{max} (cm^{-1}): 3255 (NH), 2954 (CH), 1571 (C=N), 1753 (C=O), 1030 (C–N); ^{1}H NMR ($CDCl_3$, δ ppm): 3.02 (s, 6H, CH_3) 3.04-3.10 (dd, 1H, *J=3.6, 17.1Hz*, C_4-H_a), 3.72-3.80 (dd, 1H, *J=12.1, 16.9Hz*, C_4-H_b), 3.84 (s, 3H, OCH_3), 5.97-6.05 (dd, 1H, *J=3.2, 11.0Hz*, C_5-H), 6.18 (s, 2H, NH_2), 6.71-6.75 (m, 2H, Ar-H), 6.88-7.07 (m, 4H, Ar-H), 7.14-7.237 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.32 (2C, CH_3), 42.30 (1C, C-4), 55.82 (1C),

55.10 (1C), 65.14 (1C, C-5), 115.92 (2C), 125.10 (1C), 125.66 (1C), 128.66 (2C), 126.18 (2C), 129.80 (1C), 131.41 (1C), 135.00 (1C), 154.15 (1C, C-3), 153.90 (1C), 154.43 (1C, C=O). MS (*m/z*): 338.17 (M+, 100); Anal. Calcd. for $C_{19}H_{22}N_4O_2$ (%): C, 67.44; H, 6.55; N, 16.56; Found: C, 67.38; H, 6.49; N, 16.49.

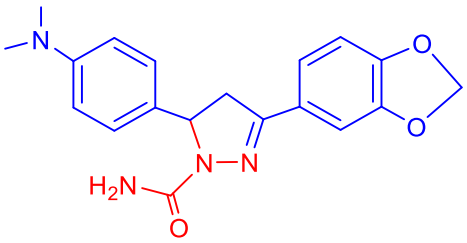
5.5.7 5-(4-(dimethylamino)phenyl)-3-(3-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5f



Obtained from 3-(4-(dimethylamino)phenyl)-1-(4-methoxyphenyl)prop-2-en-1-one, **3e** (2.81g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 75% yield, m.p. 174-177 °C.

IR (KBr) ν_{max} (cm^{-1}): 3253 (NH), 2962 (CH), 1568 (C=N), 1674 (C=O). ^{1}H NMR ($CDCl_3$, δ ppm): 3.02 (s, 6H, CH_3), (3.05-3.10 (dd, 1H, *J=3.2, 17.6Hz*, C_4-H_a), 3.75 (s, 3H, OCH_3), 3.76-3.83 (dd, 1H, *J=12.1, 17.2Hz*, C_4-H_b), 5.96-6.00 (dd, 1H, *J=3.5, 11.0Hz*, C_5-H), 6.21 (s, 2H, NH_2), 6.87-6.99 (m, 2H, Ar-H), 7.07 (m, 1H, Ar-H), 7.31 (s, 1H, Ar-H), -7.996 (m, 4H, Ar-H) 7.784-7.996 (m, 3H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.35 (2C, CH_3), 42.34 (1C, C-4), 55.85 (1C), 55.14 (1C), 65.18 (1C, C-5), 115.96 (2C), 125.14 (1C), 125.69 (1C), 128.68 (2C), 126.20 (2C), 129.86 (1C), 131.43 (1C), 135.10 (1C), 154.19 (1C, C-3), 153.93 (1C), 154.46 (1C, C=O). MS (*m/z*): 338.17 (M+, 34); Anal. Calcd. for $C_{19}H_{22}N_4O_2$ (%): C, 67.44; H, 6.55; N, 16.56; Found: C, 67.39; H, 6.49; N, 16.50.

5.5.8 3-(benzo[d][1,3]dioxol-5-yl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, 5g



Obtained from 1-(benzo[d][1,3]dioxol-5-yl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one, **3g** (2.95g, 10 mmol) and semicarbazide hydrochloride, **4** (1.11g, 10 mmol) in 72% yield, m.p. 258-260 °C.

IR (KBr) ν_{max} (cm^{-1}): 3253 (NH), 2952 (CH), 1570 (C=N), 1740 (C=0); ^{1}H NMR ($CDCl_3$, δ ppm): 3.05 (s, 6H, CH_3), 3.05-3.10 (dd, 1H, *J=3.2, 17.6Hz*, C_4-H_a), 3.76-3.83 (dd, 1H, *J=12.1, 17.2Hz*, C_4-H_b), 5.96-6.02 (dd, 1H, *J=3.5, 11.0Hz*, C_5-H), 6.06 (s, $O_2(CH_2)$), 6.212 (s, 2H, NH_2), 6.87-6.99 (m, 2H, Ar-H), 7.40 (s, 1H, Ar-H), 7.784-

7.996 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 41.3 (2C), 42.36 (1C, C-4), 66.10 (1C, C-5), 101.2 (1C), 111.9 (1C), 101.4 (1C), 122.92 (2C), 123.60 (2C), 125.11 (1C), 125.65 (1C), 126.15 (1C), 129.85 (1C), 145.00 (1C), 147.90 (1C), 154.12 (1C, C-3), 183.98 (1C, C=O). MS (*m/z*): 352.14 (M+, 100), 353.13 (M+1, 10); Anal. Calcd. for $C_{19}H_{20}N_4O_3$ (%): C, 64.76; H, 5.72; N, 15.90; Found: C, 64.71; H, 5.67; N, 15.86.

5.6 Antioxidant activity synthesised compounds

The newly synthesized pyrazol-1-carboxamide series of compounds 5(**a-g**) have been evaluated in vitro for their antioxidant properties. The DPPH radical scavenging ability of the synthesized compounds **5(a-g)** was performed by Blois method [21]. The experiments were performed with different aliquots of test samples (25, 50, 75 and 100 µg mL-1) in methanol and therefore, the absorbance was read against blank at 517 nm in an Elico SL 159 UV visible spectrophotometer. Amongst the methods available in the literature, 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay (Blois method) was adopted to evaluate the antioxidant properties of the synthesized compounds. The DPPH radical scavenging ability of the synthesized compounds **5**(**a-g**) were performed by a reported. The experiments were performed in triplicate at four different concentrations; the results were taken as a mean ± standard deviation (SD). The results of DPPH radical scavenging activities of the synthesized compounds **5**(**a-g**) are given in **Table 5.1**.

Table 5.1: DPPH radical scavenging activity of the compounds **5**(**a-g**)

Compound	% Radical Scavenging activity*			
	25 (µg/mL)	50 (µg/mL)	75 (µg/mL)	100 (µg/mL)
5a	18.10 ± 0.40	22.40 ± 0.60	27.30 ± 0.45	39.10 ± 0.40
5b	19.20 ± 0.50	20.20 ± 0.55	26.20 ± 0.50	31.45 ± 0.30
5c	18.95 ± 0.40	19.85 ± 0.50	23.60 ± 0.30	26.25 ± 0.40
5d	20.55 ± 0.20	21.15 ± 0.40	29.50 ± 0.70	32.10 ± 0.50
5e	24.70 ± 0.55	29.90 ± 0.80	48.40 ± 0.80	49.60 ± 0.70
5f	29.75 ± 0.45	34.70 ± 0.70	50.40 ± 0.80	50.60 ± 1.00
5g	21.60 ± 0.50	23.80 ± 0.60	27.81 ± 0.55	35.10 ± 0.50
AA[a]	15.10 ± 0.84	17.85 ± 0.84	23.90 ± 0.55	24.50 ± 0.30

* Values are mean ± SD (n=3); [a]Ascorbic acid used as a standard antioxidant

Based on the experimental results, it was observed that all the synthesized series of compounds **5**(**a-g**) showed broad range of good to moderate *in vitro* DPPH radical scavenging abilities. Compounds 3-(4-chlorophenyl)-5-

(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, **5c** and Interestingly, the results were incidentally similar to those demonstrated by the standard ascorbic acid used in the experiment.

Promising radical scavenging abilities have been shown by the compounds 5-(4-(dimethylamino)phenyl)-3-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide, **5a** in the range of (18.10-39.10 µg/mL); 5-(4-(dimethylamino)phenyl)-3-(4-fluorophenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, **5b** in the range of (19.20-31.45 µg/mL); 3-(benzo[d][1,3]dioxol-5-yl)-5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazole-1-carboxamide, **5g** in the range of (21.60-35.10 µg/mL); at the tested sample concentrations.

5.7 Conclusion

In the present work, we developed a new, environmentally benign, simple and reliable procedure for synthesis of pyrazole carboxamides from various tertiary amine tethered chalcones. Structures of synthesized new pyrazole carboxamides were confirmed by spectral studies, elemental analysis. Amongst the synthesized series compounds **5c**, and **5g** exhibited excellent DPPH radical scavenging abilities in comparison with the standard ascorbic acid. Further, preliminary studies show that compounds **5c** excellent antioxidant activities. The compounds **5a**, **5b** and **5g** possess promising DPPH radical scavenging abilities.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.
Author contribution:
Penubolu Sudeep: Methodology, Investigation, Writing-original draft
Dinesh Kumar Govindappa : Investigation
Dileep kumar Achutha: Investigation, antioxidant activity
Prof. Ajay Kumar Kariyappa: Investigation, Supervision, Writing-review and editing

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