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Original article

Microwave synthesis, characterization and bio-efficacy evaluation of novel chalcone based 6-carbethoxy-2-cyclohexen-1-one and 2H-indazol-3-ol derivatives

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ABSTRACT

Novel chalcone based 6-carbethoxy-2-cyclohexen-1-one and 2H-indazol-3-ol derivatives were synthesized and characterized by using spectral techniques like IR, ^{1}H NMR, ^{13}C NMR, COSY, DEPT, and GC-MS. All these compounds were screened for anti-fungal, anti-bacterial and anti-oxidant activity. Cyclohexenone derivatives, in general, showed better anti-fungal and anti-bacterial activity than parent chalcones. Whereas, all the Indazole derivatives showed very good anti-oxidant activity and some were also found to be active as anti-bacterial agent. Among the screened compounds, **15** was found to be most active as anti-fungal agent (against *Rhizoctonia solani*, $LC_{50} = 2.36$ μg mL^{-1}), **15b** was found to be most active anti-bacterial agent (against *Klebsiella pneumonia*, MIC = 24.68 μg mL^{-1}) and **14b** emerged as most active anti-oxidant ($IC_{50} = 19.81$ μg mL^{-1}).

1. Introduction

Due to stringent and growing environmental regulations, the chemical industry needs the development of more eco-compatible synthetic methodologies and consequently a detailed re-examination of the important synthetic processes [1]. In recent decades, microwave heating has taken an incontestable place in analytical and organic laboratories practice as a very effective and non-polluting method of activation.

Microwave irradiation leads to large reduction in reaction time, enhancement in conversion, and sometimes [2,3] in selectivity with several advantages of the environmental approach, termed green chemistry. The solvent-free Microwave assisted reactions [4] have gained popularity as they provide potentialities to work with open vessels and enhanced possibility of up-scaling the reactions on preparative scale [4–6].

Chalcone is a generic term for the compounds bearing the 1, 3-diphenyl-prop-2-en-1-one framework [7]. Under homogeneous conditions, these compounds are usually prepared by base or acid catalyzed aldol condensation between aromatic aldehydes and ketones. Chalcones represent an important class of compounds due to their chemical flexibility, as synthons for the production of five- and six-member ring systems [8,9] for example Pyrazoles [10], Pyrazolines [11], isoxazolines [12], aurones [13], pyrimidine [14], falvanones [15] and di-aryl cyclohexenones [16]. The biological activities of chalcones are equally wide ranging [17–20]. In fact, not many structural templates can claim association with such a diverse range of pharmacological activities, among which anti-microbial [21], anti-leishmanial [22], anti-malarial [23], anti-fungal [24], anti-viral [25], anti-inflammatory [26], cytotoxicity [27], anti-tumor [28], nematicidal [29] and anti-oxidant [30] are widely cited.

From a chemical point of view, an important feature of chalcones and their hetero-analogs is the ability to act as activated unsaturated systems in conjugated addition reactions of carbanions in the presence of basic catalysts [31,32]. This type of reaction is more commonly used for the preparation of 3,5-diaryl-6-carbethoxycyclohexenones via Michael addition of ethyl

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acetoacetate [33–35]. The mentioned cyclohexenones are efficient synthons in building spiranic compounds [36] or intermediates in the synthesis of fused heterocycles such as benzoselenadiazoles and benzothiadiazoles [37], benzopyrazoles and benzisoxazoles [38,39], carbazole derivatives [40], and 2H-indazoles [41].

The anti-bacterial, anti-fungal, anti-cancer and anti-tubercular activities of di-arylcyclohexenone derivatives were also reported [42,43].

Wide spectrum of biological activities has been reported for indazoles and they have increasingly attracted the attention in pharmaceutical field due to various interesting bioactivity against different targets [44,45].

In the quest for biologically more potent anti-microbial and anti-oxidant agents and to increase the molecular diversity, we envisioned to design and synthesize the chalcone based 6-Carbethoxy-2-cyclohexen-1-one and 2H-Indazol-3-ol Derivatives through a simple, efficient and environment friendly method which utilizes the approach of "*Green chemistry*".

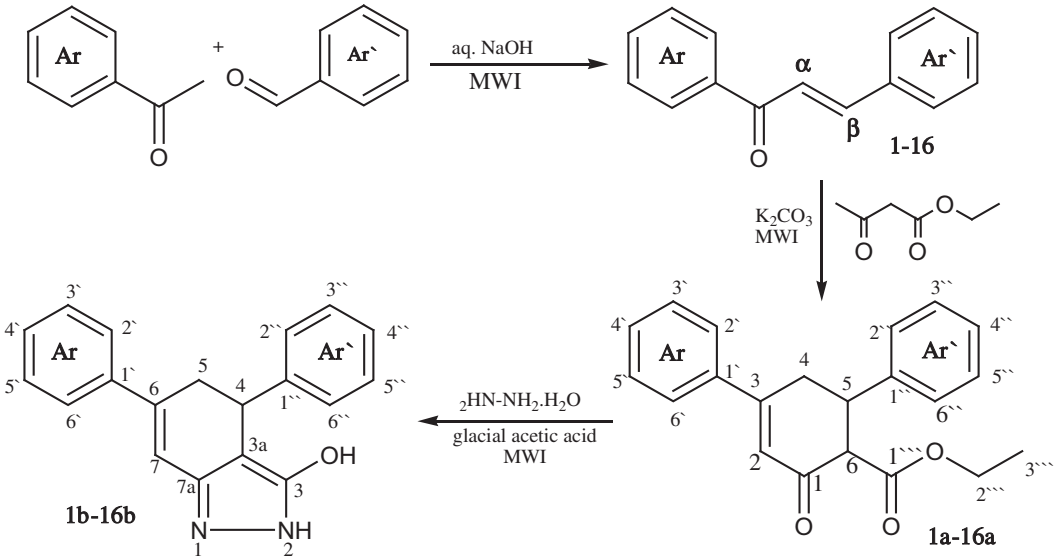
2. Results and discussion

2.1. Chemistry

Chalcones (**1**–**16**) were prepared from substituted acetophenones and benzaldehydes using aq. NaOH under microwave irradiation. The chalcones were then condensed with ethyl acetoacetate using K_2CO_3, under microwave irradiation to give cyclohexenones (**1a**–**16a**). These cyclohexenones were then condensed with hydrazine hydrate in presence of glacial acetic acid under microwave irradiation to afford 2H-indazol-3-ols (**1b**–**16b**) (Scheme 1). All the cyclohexenone and indazole derivatives were characterized by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR, COSY, DEPT, and GC-MS.

Claisen-Schmidt condensation method for the synthesis of chalcones is very attractive since it specifically generates the *trans* (E)-isomer [8,46,47]. Signals for two vinylic protons in the structure of chalcones appear as two doublets in aromatic region of ^{1}H NMR spectra, and their coupling constant (J) showed that all chalcones were geometrically pure and with *trans*-configuration ($J_{H\alpha-H\beta}$ = 15.50–16.50 Hz). Aromatic protons appear between δ 6.9 and 8.1. In ^{13}C NMR, a signal at around δ 190 confirms the presence of carbonyl group. Signal for α and β carbons appear at around δ 145 and 120 respectively. Aromatic carbons appear at around δ 120–140. The IR spectrum supported the NMR data showing the characteristic band for C]O at 1655–1660 and C]C Ar at around 1600 and 1475 cm^{-1}.

The cyclo-condensation of ethyl acetoacetate with chalcones leads to the generation of two chiral centers at C-5 and C-6 in the structure of cyclohexenones. As the explored reaction is not stereo selective, both configurations of the chiral carbon atoms are expected to be noticed in the synthesized cyclohexenones, which would result in a mixture of diastereomers. No attempt to separate the diastereomeric cyclohexenones was undertaken, and the cyclo-condensation products have been characterized in the form of the mixture originated from the synthesis. The IR spectra of these compounds revealed a sharp strong absorption band above 1700 cm^{-1} that can be correlated with the presence of the ester function in the structure of cyclohexenones. Furthermore, another sharp strong absorption band was noticed at approximately 1660 cm^{-1} and was assigned to the carbonyl group conjugated with a carbon–carbon double bond. No other absorption band could be evidenced in the region of the IR spectrum associated with the stretching vibrations of the carbonyl group, thus excluding the intermediate Michael adduct having an extra carbonyl group. The ^{1}H NMR spectra substantiated the results of the IR analysis. The characteristic signals of an ethyl ester moiety (a triplet at chemical shift values of about δ 1 and a quartet at around δ 4) confirmed the presence of the ester group in the structure of cyclohexenones. The characteristic signal in the ^{1}H NMR spectrum was however the singlet of the vinylic proton of the cyclohexenone ring, that appeared at approximately δ 6.5 and confirming that the intramolecular cyclo-condensation, subsequent to the Michael addition, actually took place. The two protons at C-4, being non-equivalent, appeared as two different signals, the axial proton appeared as double of double-doublet at around δ 2.95 showing both germinal coupling, vicinal coupling and long range ^{1}H–^{1}H coupling and the equatorial proton appeared as double-doublet at around δ 3.05, showing germinal and vicinal couplings. The signals for the protons at C-5 and C-6 appeared as a multiplet at around δ 3.7. Vinylic proton at C-2 appeared as doublet at around δ 6.5 and aromatic protons appeared between δ 6.7 and 7.8. COSY spectrum of cyclohexenones confirmed the long range ^{1}H–^{1}H coupling between axial proton at C-4 and vinylic proton at C-2. ^{13}C NMR also



Scheme 1. General method for the synthesis of cyclohexenone and indazole derivatives.

supported the above data showing two signals at around δ 170 and 195 due to carbonyl carbons and a signal at around δ 158 for quaternary vinylic carbon (C-3).

Treatment of cyclohexenones **1a**–**16a** with hydrazine hydrate in presence of ethanolic acetic acid gave the corresponding indazole derivatives **1b**–**16b** which can be tautomeric mixtures [48] (Fig. 1).

The absence of carbonyl bands in the IR spectra of the products ruled out lactam structures **A** and **B**. The ^{1}H NMR spectra exhibited three protons in the sp^3 shift range (H-5$_{eq}$, H-5$_{ax}$ and H-4). H-5$_{eq}$ and H-4 appeared as double-doublets at around δ 2.90 and 4.18 respectively while, the signal for H-5$_{ax}$ appeared as double of double-doublet at around δ 3.17 showing geminal coupling with H-5$_{eq}$, vicinal coupling with H-4 and long range proton coupling with H-7. Protons that exchanged with D_2O at around δ 9.7 were assigned to OH and NH. Aromatic protons appeared between δ 7 and 8 and a doublet at around δ 6.7 was due to vinylic proton H-7. A cross peak in the COSY spectrum confirmed the long range ^{1}H-^{1}H coupling between H-5$_{ax}$ and H-7. On the other hand, the ^{13}C NMR spectra of these compounds showed signal at around δ 156 due to C-3. Signals for other quaternary carbons and aromatic carbons appeared at around δ 125–145. The signal for vinylic carbon C-7 appeared at around δ 113. In ^{13}C NMR of indazoles, a signal at δ 98–99 can be attributed to a sp^2-hybridized carbon atom (C-3a) that shifted to high field. DEPT experiments also support the ^{1}H and ^{13}C NMR data. The tautomer **C** was therefore assigned as the sole component of indazole derivative formed.

2.1.1. Microwave method Vs conventional method

Chalcones (**1**–**16**), cyclohexenones (**1a**–**16a**) and indazoles (**1b**–**16b**) were synthesized using self designed microwave method and already reported non-microwave method [43]. Table 1 summarizes the comparison of two methods in terms of reaction time and yield and emphasizes the advantages of microwave reaction in addition to solvent less conditions, increased conversion etc.

2.2. Bio-efficacy evaluation

2.2.1. Fungicidal activity

All the synthesized compounds were tested for their fungicidal activity against two phyto-pathogenic fungi *Rhizoctonia solani* and *Sclerotium rolfsii*. Both are known pests on number of plants. The inhibitory effects of synthesized compounds on the growth of test fungi were expressed in terms of 50% lethal concentration (LC_{50}). None of the indazole derivative was found to be active against both *R. solani* and *S. rolfsii*. LC_{50} values for indazoles ranged from 713–1241 mg L^{-1} for *S. rolfsii* and 528–1034 mg L^{-1} for *R. solani* (Table 2). Results for anti-fungal activity were summarized in Table 2 which indicate that the synthesized compounds were comparatively more active against *R. solani* than *S. rolfsii*. Also, against *S. rolfsii* the cyclohexenones were more active than the parent chalcones except for compounds **9** and **12**. However, no such generalization was possible when compounds were tested against *R. solani*. The compounds i.e., 1-(4-Fluorophenyl)-3-phenyl-propenone (**15**) and 1,3-Diphenyl-propenone (**16**) were highly effective as fungicide against *R. solani* with LC_{50} values 2.36 and 2.49 mg L^{-1} respectively, comparable with that of commercial fungicide Hexaconazole (LC_{50} 1.27 mg L^{-1} and 1.12 mg L^{-1} against *S. rolfsii* and *R. solani* respectively).

2.2.2. Anti-bacterial activity

All the synthesized compounds (100 μg/disk) were screened for their anti-bacterial activity using disk diffusion method, against two gram positive beneficial bacteria, *Bacillus thuringiensis* and *Bacillus pumilis*, two gram negative plant pathogens, *Erwinia chrysanthemi* and *Xanthomonas oryzae* and three human pathogens, *Klebsiella pneumonia* (gram negative), *Staphylococcus aureus* (gram positive) and *Pseudomonas aeruginosa* (gram negative). Dimethyl sulfoxide was used as control and Streptomycin, Ampicillin and Kanamycin (25 μg/disk) were used as positive control.

All the synthesized compounds were found to be inactive against beneficial bacteria, *B. thuringiensis* and *B. pumilis*, giving an idea that they were target specific and not toxic to beneficial microbes. Also, all the compounds were found to be inactive against *X. oryzae* (Table 3).

Against *E. chrysanthemi*, compounds **3a** and **11a** showed good activity (zone of inhibition = 15–20 mm) where as compounds **14**, **16**, **9a**, **13a**, **14a** and **15a** showed moderate activity (zone of inhibition = 10–15 mm). Against *Klebsiella pneumonia*, compound **15b** showed good anti-bacterial activity (zone of inhibition = 15–20 mm) and compounds **6a**, **15a** and **16a** showed moderate activity (zone of inhibition = 10–15 mm). All the synthesized chalcones were found to be inactive against *K. pneumonia*. Against *S. aureus*, compounds **16**, **2b** and **16b** showed poor to moderate activity (zone of inhibition = 5–10 mm) and all the other synthesized compounds were found to be inactive. Against *P. aeruginosa*, compounds **16**, **6a**, **2b** and **6b** showed moderate to good activity (zone of inhibition = 10–15 mm) where as compounds **1a** and **1b** showed poor to moderate activity (zone of inhibition = 5–10 mm). Streptomycin was found to be most active antibiotic against all the test bacteria (Table 3).

Compounds **3a** and **11a** showed good activity against *E. chrysanthemi* and **15b** showed good activity against *K. pneumonia.* These compounds were subjected to the anti-bacterial screening using broth dilution technique. Streptomycin drug was used as the standard. The minimum inhibitory concentration (MIC) was noted by observing the lowest concentration of the drug at which there was more than 90% inhibition of bacteria. The results are listed in Table 4.

The investigation of anti-bacterial screening using broth dilution technique revealed that all the three compounds **3a** (55.9 μg/mL against *E. chrysanthemi*), **11a** (73.6 μg/mL against *E. chrysanthemi*) and **15b** (24.68 μg/mL against *K. pneumonia*) showed moderate to good bacterial inhibition as compared to the standard drug streptomycin (4.6 μg/mL against *E. chrysanthemi* and 3.1 μg/mL against *K. pneumonia*).

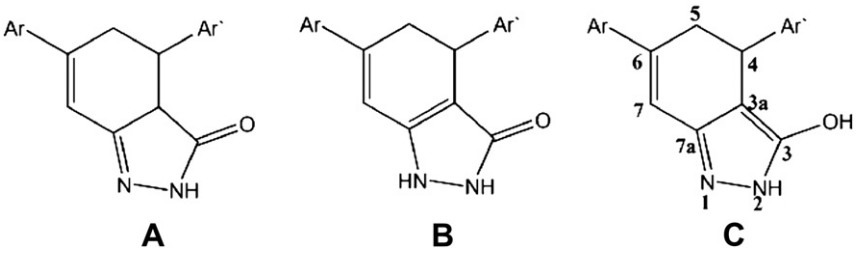


Fig. 1. Tautomeric forms of 2H-indazol-3-ol.

Table 1
Comparison of microwave and conventional (non-microwave) methods used for the synthesis of chalcone, cyclohexenone and indazole derivatives.

Compound	Parameter				
	Reaction time		Yield (%)		
	Conventional method [43]	Microwave method	Conventional method	Microwave method	Increase
Chalcones	24 h	5–7 min	55–89	71–96	6–14
Cyclohexenones	5 h	6–8 min	60–91	62–95	3–7
Indazoles	6 h	3 min	54–82	69–93	9–16

2.2.3. Anti-oxidant activity

A simple method was used to determine the anti-oxidant activity of synthesized compounds. It utilizes the stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. The odd electron in the DPPH free radical gave a strong absorption maximum at 517 nm and was purple in color. The color turned from purple to yellow as the molar absorptivity of the DPPH radical at 517 nm reduces when the odd electron of DPPH radical becomes paired with hydrogen from a free radical scavenging anti-oxidant to form the reduced DPPH-H. The resulting decolorization is stoichiometric with respect to number of electrons captured.

All the synthesized compounds were first screened for their free radical scavenging activity. Out of all the compounds tested, only 2H-indazol-3-ol series was found to be significantly active as anti-oxidants (Table 5). Anti-oxidant activity of indazoles was then tested at different concentration viz., 10, 20, 40, 60, 80, 100, 200, 300, 400 and 500 μg mL^{-1} (Table 6, Fig. 2). The free radical scavenging power of indazoles can be attributed to the presence of –OH and –NH groups in their structure.

It was very clear from Table 6 that with the increase in concentration, the free radical scavenging activity of compounds also increased. Also, once around ninety percent of inhibition was achieved, the increase in concentration of compounds had no significant effect on the free radical scavenging activity and it reached a plateau (Table 6). This might be because the concentration of anti-oxidant in the solution reaches a level where steric hindrance (intermolecular interactions) comes into play and anti-oxidant compound was not able to donate its electron to DPPH radical.

Free radical scavenging activity of synthesized indazoles in terms of 50% inhibitory concentration (IC_{50}) was summarized in Table 7. Among all the indazoles tested, 6-(4-fluorophenyl)-4,5-dihydro-4-(3-nitrophenyl)-2H-indazol-3-ol (**14b**) was highly effective as anti-oxidant with IC_{50} value 19.81 μg mL^{-1} compared to IC_{50} value 1.28 μg mL^{-1} for gallic acid.

Table 2
Anti-fungal activity of chalcone (**1**–**16**), cyclohexenone (**1a**–**16a**) and indazole (**1b**–**16b**) derivatives; LC_{50} (mg L^{-1}).

Anti-fungal activity[a]								
Chalcones			Cyclohexenones			Indazoles		
	S.r.[b]	*R.s* [b]		*S.r.*	*R.s.*		*S.r.*	*R.s.*
1	601	109	**1a**	323	198	**1b**	817	696
2	541	662	**2a**	316	233	**2b**	922	745
3	628	1369	**3a**	347	116	**3b**	713	718
4	599	421	**4a**	365	139	**4b**	1024	917
5	587	107	**5a**	317	189	**5b**	939	861
6	549	635	**6a**	321	231	**6b**	876	814
7	631	1275	**7a**	345	118	**7b**	1173	738
8	605	663	**8a**	315	**34**	**8b**	1241	1034
9	623	441	**9a**	4308	**29**	**9b**	963	931
10	677	375	**10a**	380	396	**10b**	897	643
11	679	451	**11a**	372	**58**	**11b**	941	587
12	664	**52**	**12a**	6113	1044	**12b**	1031	776
13	717	238	**13a**	504	–	**13b**	894	611
14	757	**65**	**14a**	285	157	**14b**	796	528
15	522	**2.36**	**15a**	319	**35**	**15b**	912	669
16	674	**2.49**	**16a**	304	207	**16b**	873	802
Hx[b]	1.27	1.12						

[a] Anti-fungal activity of some chalcones and cyclohexenones were reproduced from our previous publication [49].
[b] *S.r* = *Sclerotium rolfsii* and *R.s* = *Rhizoctonia solani*; Hx. = Hexaconazole.

3. Experimental

3.1. Chemicals and instruments

All the chemicals used were purchased from Sigma–Aldrich and were used without further purification. Analytical grade reagents and solvents were locally procured and used as such. Reactions were monitored by thin layer chromatography (TLC) on pre-coated Merck silica gel $60F_{254}$, 200 μm thick aluminum sheets and the spots were visualized either under UV or by iodine vapor. Column chromatography (CC) was carried out on silica gel (Merck, 100–200 mesh). House-hold microwave, LG-MG607APR was used at full power (900 W) for carrying out chemical reactions. Melting points were determined on a JSW melting point apparatus and were reported uncorrected. The ^1H NMR, COSY, ^{13}C NMR and DEPT spectra were recorded on Bruker 400 MHz Spectrospin spectrometer, using tetramethylsilane (TMS) as an internal standard. The chemical shift values were recorded on δ scale and the coupling constants (J) are in Hz. Infrared (IR) spectra were recorded on Bruker alpha FT-IR spectrophotometer using Attenuated Total Reflectance (ATR) technique and values are expressed as ν_{max} cm^{-1}. Mass spectra were recorded on a Thermo Fisher GC-MS, equipped with Focus GC, DSQ II mass spectrometer and Triplus auto sampler. Thermo TR-5 MS capillary column (30 m × 0.25 mm × 0.25 μm) was used in Focus GC. Elemental analyses for all compounds were performed on a Carlo Erba Model EA-1108 elemental analyzer. Anti-oxidant activity was done using UV–Visible spectrophotometer Specord 200 Analytik Jena GmbH, Germany. A computer based program, GWBASIC/Indostat, was used to calculate LC_{50} and IC_{50} values.

3.2. General procedure for the synthesis of chalcones (*1*–*16*) [49]

Selected acetophenone (10 mmol) and selected benzaldehyde (10 mmol) were added to 50 ml of 5% aqueous NaOH. The mixture was placed in the centre of microwave oven besides a beaker with ice (50 g) and irradiated for successive periods of 10 s, 5–7 min in total, with cooling in between. After irradiation, color of the mixture changed to crimson. The mixture was then poured into 200 ml of ice cold water and neutralized with cold HCl. The precipitate formed was filtered and recrystallized with ethanol to afford the chalcones namely (*E*)-3-(3,4-Dimethoxyphenyl)-1-phenyl-propenone (**1**), (*E*)-1-Phenyl-3-*p*-tolyl-propenone (**2**), (*E*)-3-(4-Methoxyphenyl)-1-phenyl-propenone (**3**), (*E*)-3-(3,4,5-Trimethoxy-phenyl)-1-phenyl-propenone (**4**), (*E*)-3-(3,4-Dimethoxyphenyl)-1-*p*-tolylprop-2-en-1-one (**5**), (*E*)-1,3-Di-*p*-tolyl-prop-2-en-1-one (**6**), (*E*)-3-(3,4,5-Trimethoxyphenyl)-1-*p*-tolylprop-2-en-1-one (**7**), (*E*)-3-(3,4-Dimethoxyphenyl)-1-(4-methoxyphenyl)-propenone (**8**), (*E*)-3-Benzo[1,3]dioxol-5-yl-1-(4-nitrophenyl)-propenone (**9**), (*E*)-1-Benzo[1,3]dioxol-5-yl-3-(4-methoxyphenyl)-

Table 3
Anti-bacterial activity of chalcone (**1**–**16**), cyclohexenone (**1a**–**16a**) and indazole (**1b**–**16b**) derivatives.

Compounds[a]	Beneficial bacteria		Plant pathogen		Human pathogen		
	B.t[a]	*B.p*[a]	*E.c*[a]	*X.o*[a]	*K.p*[a]	*S.a*[a]	*P.a*[a]
Streptomycin	+ + + +	+ + +	+ + + +	+ + + +	+ + + +	+ + + +	+ + + +
Ampicillin	–	+ + + +	+ + + +	+	+ +	+ +	+ +
Kanamycin	+ + +	–	–	–	+ + +	+ +	–
DMSO	–	–	–	–	–	–	–
1	–	–	–	–	–	–	–
2	–	–	–	–	–	–	–
3	–	–	–	–	–	–	–
4	–	–	–	–	–	–	–
5	–	–	–	–	–	–	–
6	–	–	–	–	–	–	–
7	–	–	–	–	–	–	–
8	–	–	–	–	–	–	–
9	–	–	–	–	–	–	–
10	–	–	–	–	–	–	–
11	–	–	–	–	–	–	–
12	–	–	–	–	–	–	–
13	–	–	–	–	–	–	–
14	–	–	+ +	–	–	–	–
15	–	–	–	–	–	–	–
16	–	–	+ +	–	–	+	+ +
1a	–	–	–	–	–	–	+
2a	–	–	–	–	+	–	–
3a	–	–	+ + +	–	–	–	–
4a	–	–	–	–	–	–	–
5a	–	–	–	–	–	–	–
6a	–	–	–	–	+	–	+ +
7a	–	–	–	–	–	–	–
8a	–	–	–	–	–	–	–
9a	–	–	+ +	–	–	–	–
10a	–	–	–	–	–	–	–
11a	–	–	+ + +	–	–	–	–
12a	–	–	–	–	–	–	–
13a	–	–	+ +	–	–	–	–
14a	–	–	+ +	–	–	–	–
15a	–	–	+ +	–	+ +	–	–
16a	–	–	–	–	+ +	–	–
1b	–	–	–	–	–	–	+
2b	–	–	–	–	–	+	+ +
3b	–	–	–	–	–	–	–
4b	–	–	–	–	–	–	–
5b	–	–	–	–	–	–	–
6b	–	–	–	–	–	+	+ +
7b	–	–	–	–	–	–	–
8b	–	–	–	–	–	–	–
9b	–	–	–	–	–	–	–
10b	–	–	–	–	–	–	–
11b	–	–	–	–	–	–	–
12b	–	–	–	–	–	–	–
13b	–	–	–	–	–	–	–
14b	–	–	–	–	–	–	–
15b	–	–	–	–	+ + +	–	–
16b	–	–	–	–	+ +	–	–

[a] All the synthesized compounds and DMSO were tested at 100 μg/disk. Streptomycin, Ampicillin and Kanamycin were tested at 25 μg/disk. Zone of inhibition: (–) 0–5 mm, inactive; (+) 5–10 mm, poor activity; (+ +) 10–15 mm, moderate activity; (+ + +) 15–20 mm, good activity and (+ + + +) 20–25 mm, very good activity. *B.t* – *Bacillus thuringiensis*, *B.p* – *Bacillus pumilis*, *E.c* – *Erwinia chrysanthemi*, *X.o* – *Xanthomonas oryzae*, *K.p* – *Klebsiella pneumonia*, *S.a* – *Staphylococcus aureus* and *P.a* – *Pseudomonas aeruginosa*.

propenone (**10**), (*E*)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)-propenone (**11**), (*E*)-1-(3,4-Dichlorophenyl)-3-(4-methoxyphenyl)-propenone (**12**), (*E*)-1-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)-propenone (**13**), (*E*)-1-(4-Fluorophenyl)-3-(3-nitrophenyl)-propenone (**14**), (*E*)-1-(4-Fluorophenyl)-3-phenyl-propenone (**15**) and (*E*)-1,3-Diphenyl-propenone (**16**).

Table 4
Anti-bacterial screening of compounds **3a**, **11a** and **15b** using Broth Dilution Technique.

Compound	Bacteria	MIC (μg/mL)
3a	*E. chrysanthemi*	55.9
11a	*E. chrysanthemi*	73.6
15b	*K. pneumonia*	24.68
Streptomycin	*E. chrysanthemi*	4.6
Streptomycin	*K. pneumonia*	3.1

3.3. General procedure for the synthesis of cyclohexenones (*1a*–*16a*) [49]

To a slurry of chalcone (10 mmol) and ethyl acetoacetate (20 mmol) anhydrous K_2CO_3 (40 mmol) and silica (2 g) was added and mixed thoroughly. The mixture was air dried and subjected to microwave irradiation for 6–8 min with 30 s pulse and cooling in between. After completion of reaction as indicated by TLC, the reaction mixture was cooled to room temperature and extracted with ethanol. The in-organics were filtered off. On standing the

Table 5
Anti-oxidant activity of chalcone (**1**–**16**), cyclohexenone (**1a**–**16a**) and indazole (**1b**–**16b**) derivatives at 40 μL of stock solution.

Anti-oxidant activity (%) (concentration = 40 μL stock)					
Chalcones		Cyclohexenones		Indazoles	
1	0.81	**1a**	4.23	**1b**	69.87
2	1.06	**2a**	4.17	**2b**	18.21
3	1.33	**3a**	2.69	**3b**	50.25
4	0.77	**4a**	1.69	**4b**	67.1
5	0.71	**5a**	7.38	**5b**	62.60
6	1.19	**6a**	3.54	**6b**	18.15
7	−0.65	**7a**	4.52	**7b**	56.86
8	0.56	**8a**	4.71	**8b**	65.33
9	0.68	**9a**	3.60	**9b**	19.81
10	0.73	**10a**	4.26	**10b**	56.09
11	0.65	**11a**	4.74	**11b**	43.16
12	0.48	**12a**	2.92	**12b**	48.55
13	0.81	**13a**	11.30	**13b**	12.80
14	0.77	**14a**	4.23	**14b**	67.86
15	4.03	**15a**	3.86	**15b**	70.48
16	9.11	**16a**	3.33	**16b**	40.27
Gallic acid	21.4				

filtrate afforded crystals of cyclohexenones (**1a**–**16a**). All the products were characterized by IR, NMR and mass spectra.

3.3.1. 5-(3,4-Dimethoxyphenyl)-3-phenyl-6-carbethoxy-2-cyclohexen-1-one (*1a*)

White solid. M.P.: 126 °C. Yield: 88%. IR (ATR, cm^{-1}): 1743, 1659. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.93 (3H, t, H-3‴, J = 6.8 Hz), 2.96 (1H, ddd, H-4ax, J = 1.6, 4.8 and 14.2 Hz), 3.07 (1H, dd, H-4eq, J = 4.8 and 14.2 Hz), 3.66 (2H, m, H-5 and H-6), 3.85 and 3.87 (6H, 2s, Ar-OCH_3), 3.92 (2H, q, H-2‴, J = 6.8 Hz), 6.56 (1H, d, H-2, J = 1.6 Hz), 6.80–6.87 (3H, m, H-2″, H-5″ and H-6″), 7.19–7.25 (3H, m, H-3′, H-4′ and H-5′), 7.44 (2H, d, H-2′ and H-6′, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C-3‴), 36.3 (C-4), 43.9 (C-5), 55.7 (−OCH_3), 59.7 (C-6), 60.3 (C-2‴), 126.1 (C-2), 157.8 (C-3), 168.7 (C-1‴), 194.6 (C-1), 111.1, 111.9, 119.5, 124.1, 130.4, 133.6, 139.4, 141.2, 148.5 and 148.9 (Aromatic carbons). Mass (M^+): 380. Anal. Calculated for $C_{23}H_{24}O_5$: C-72.61; H-6.36%. Observed: C-72.34; H-6.59%.

3.3.2. 3-Phenyl 5-(p-tolyl)-6-carbethoxy-2-cyclohexen-1-one (*2a*)

White solid. M.P.: 142 °C. Yield: 91%. IR (ATR, cm^{-1}): 1739, 1652. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.94 (3H, t, H-3‴, J = 7.2 Hz), 2.31 (3H, s, Ar-CH_3), 2.87 (1H, ddd, H-4ax, J = 2.0, 4.6 and 14.6 Hz), 3.03 (1H, dd, H-4eq, J = 4.8 and 14.8 Hz), 3.51 (2H, m, H-5 and H-6), 3.96 (2H, q, H-2‴, J = 7.2 Hz), 6.57 (1H, d, H-2, J = 2.0 Hz), 7.09 (2H, d, H-3″ and H-5″, J = 8.4 Hz), 7.19 (2H, d, H-2″ and H-6″, J = 8.4 Hz), 7.31–7.57 (5H, m, H-2′-6′). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4 (C-3‴), 21.1 (Ar-CH_3), 36.1 (C-4), 43.4 (C-5), 59.6 (C-6), 60.2 (C-2‴), 126.7 (C-2), 159.7 (C-3), 169.8 (C-1‴), 194.5 (C-1), 122.3, 127.8, 128.9, 129.8, 134.6, 136.5, 139.2 and 141.1 (Aromatic carbons). Mass (M^+): 334. Anal. Calculated for $C_{22}H_{22}O_3$: C-79.02; H-6.03%. Observed: C-79.44; H-6.00%.

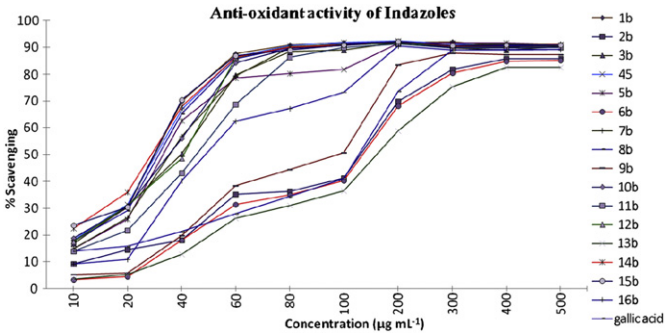


Fig. 2. Anti-oxidant activity of Indazole derivatives (**1b**–**16b**).

3.3.3. 5-(4-Methoxyphenyl)-3-phenyl-6-carbethoxy-2-cyclohexen-1-one (*3a*)

White solid. M.P.: 161 °C. Yield: 92%. IR (ATR, cm^{-1}): 1746, 1651. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (3H, t, H-3‴, J = 7.2 Hz), 2.91 (1H, ddd, H-4ax, J = 1.6, 4.8 and 14.2 Hz), 3.01 (1H, dd, H-4eq, J = 4.8 and 14.0 Hz), 3.50 (2H, m, H-5 and H-6), 3.72 (3H, s, Ar-OCH_3), 3.87 (2H, q, H-2‴, J = 7.2 Hz), 6.49 (1H, d, H-2, J = 1.6 Hz), 6.86 (2H, d, H-3″ and H-5″, J = 8.8 Hz), 7.23 (2H, d, H-2″ and H-6″, J = 8.0 Hz), 7.29–7.34 (3H, m, H-3′, H-4′ and H-5′), 7.58 (2H, d, H-2′ and H-6′, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.34 (C-3‴), 35.8 (C-4), 43.5 (C-5), 55.5 (-OCH_3), 59.5 (C-6), 60.3 (C-2‴), 126.8 (C-2), 159.7 (C-3), 169.8 (C-1‴), 194.8 (C-1), 114.2, 122.6, 129.1, 134.0, 140.9 and 158.7 (Aromatic carbons). Mass (M^+): 350. Anal. Calculated for $C_{22}H_{22}O_4$: C-75.41; H-6.33%. Observed: C-75.64; H-6.59%.

Table 6
Anti-oxidant activity of Indazole derivatives (**1b**–**16b**) at different concentrations.

Compound	Anti-oxidant activity (%) at different concentrations (μg mL^{-1})									
	10	20	40	60	80	100	200	300	400	500
1b	18.1	30.2	69.9	87.6	90.9	91.8	91.9	91.9	90.5	90.8
2b	9.2	14.5	18.2	35.1	36.4	41.2	69.9	81.8	85.7	85.7
3b	16.8	30.6	50.3	79.7	88.4	89.0	91.8	89.7	88.9	90.2
4b	18.1	31.5	67.1	86.4	90.7	91.8	92.3	91.2	90.5	90.8
5b	15.0	25.9	62.6	78.5	80.3	81.8	91.4	91.6	91.7	91.0
6b	3.4	4.4	18.2	31.5	34.9	40.3	68.1	80.5	84.8	85.2
7b	15.0	26.4	56.9	79.3	89.9	90.8	91.8	90.2	90.3	90.6
8b	17.7	29.2	65.3	85.8	90.0	91.4	92.1	90.4	90.5	90.8
9b	5.3	5.8	19.8	38.4	44.5	50.7	83.4	87.9	87.3	87.3
10b	19.0	30.4	56.1	84.2	89.5	90.7	91.9	89.8	89.9	90.1
11b	13.9	21.7	43.2	68.7	86.4	89.9	91.2	89.7	89.8	90.0
12b	17.6	31.0	48.6	86.1	90.4	91.1	91.5	90.7	91.3	91.3
13b	3.5	5.3	12.8	26.3	31.1	36.5	58.8	75.3	82.6	82.6
14b	22.6	35.9	67.9	86.4	90.1	90.8	92.3	90.5	90.9	91.1
15b	23.5	30.4	70.5	86.9	89.0	91.0	92.2	90.7	90.8	90.8
16b	9.1	10.9	40.3	62.5	67.3	73.3	90.6	89.0	89.1	89.2
Gallic acid[a]	13.9 (0.1)	15.8 (0.2)	21.4 (0.4)	28.0 (0.6)	34.4 (0.8)	41.0 (1)	73.6 (2)	88.9 (3)	89.1 (4)	89.1 (5)

[a] Values in parenthesis are concentration at which Gallic acid is tested.

Table 7
IC_{50} values for Indazole derivatives (**1b**–**16b**).

Compound	Inhibition concentration 50 percent (IC_{50}) μg mL^{-1}
1b	**21.98**
2b	106.62
3b	**29.62**
4b	**22.28**
5b	**33.12**
6b	123.54
7b	**29.7**
8b	**23.94**
9b	95.82
10b	**25.2**
11b	**42.34**
12b	**40.98**
13b	146.68
14b	**19.81**
15b	**23.71**
16b	58.28
Gallic acid	1.28

*3.3.4. 5-(3,4,5-Trimethoxyphenyl)-3-phenyl-6-carbethoxy-2-cyclohexen-1-one (**4a**)*

White solid. M.P.: 119 °C. Yield: 84%. IR (ATR, cm^{-1}): 1742, 1647. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (3H, t, H-3‴, $J = 7.2$ Hz), 2.95 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.01 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.61 (2H, m, H-5 and H-6), 3.84–3.89 (9H, 3s, Ar-OCH_3), 3.91 (2H, q, H-2‴, $J = 7.2$ Hz), 6.34 (2H, s, H-2″ and H-6″), 6.52 (1H, d, H-2, $J = 1.6$ Hz), 7.20–7.27 (3H, m, H-3′, H-4′ and H-5′), 7.45 (2H, m, H-2′ and H-6′). ^{13}C NMR ($CDCl_3$): δ 14.3 (C-3‴), 35.8 (C-4), 43.6 (C-5), 55.8 (−OCH_3), 56.0 (−OCH_3), 59.5 (C-6), 60.4 (C-2‴), 126.7 (C-2), 159.6 (C-3), 169.4 (C-1‴), 194.6 (C-1), 111.9, 112.1, 120.0, 122.6, 129.8, 134.9, 135.4, 140.8, 147.6 and 149.0 (Aromatic carbons). Mass (M^+): 410. Anal. Calculated for $C_{24}H_{26}O_6$: C-70.23; H-6.38%. Observed: C-70.44; H-6.47%.

*3.3.5. 5-(3,4-Dimethoxyphenyl)-3-(p-tolyl)-6-carbethoxy-2-cyclohexen-1-one (**5a**)*

White solid. M.P.: 152 °C. Yield: 90%. IR (ATR, cm^{-1}): 1748, 1649. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.05 (3H, t, H-3‴, $J = 7.2$ Hz), 2.36 (3H, s, Ar-CH_3), 2.90 (1H, ddd, H-4ax, $J = 2.0$, 4.8 and 14.6 Hz), 3.05 (1H, dd, H-4eq, $J = 4.8$ and 14.6 Hz), 3.70 (2H, m, H-5 and H-6), 3.85 and 3.86 (6H, 2s, Ar-OCH_3), 4.02 (2H, q, H-2‴, $J = 7.2$ Hz), 6.53 (1H, d, H-2, $J = 2.0$ Hz), 6.80–6.87 (3H, m, H-2″, H-5″ and H-6″), 7.19 (2H, d, H-3′ and H-5′, $J = 8.4$), 7.43 (2H, d, H-2′ and H-6′, $J = 8.0$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C-3‴), 21.3 (Ar-CH_3), 36.3 (C-4), 43.7 (C-5), 55.9 (−OCH_3), 59.7 (C-6), 60.9 (C-2), 126.1 (C-2), 158.6 (C-3), 169.4 (C-1‴), 194.2 (C-1), 110.5, 111.3, 119.2, 123.2, 129.6, 133.7, 134.7, 141.1, 148.2 and 148.9 (Aromatic carbons). Mass (M^+): 394. Anal. Calculated for $C_{24}H_{26}O_5$: C-73.08; H-6.64%. Observed: C-73.54; H-6.09%.

*3.3.6. 3,5-Di-(p-tolyl)-6-carbethoxy-2-cyclohexen-1-one (**6a**)*

White solid. M.P.: 148 °C. Yield: 94%. IR (ATR, cm^{-1}): 1737, 1647. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (3H, t, H-3‴, $J = 7.2$ Hz), 2.24 and 2.32 (6H, 2s, Ar-CH_3), 2.92 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.00 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.53 (2H, m, H-5 and H-6), 3.87 (2H, q, H-2‴, $J = 7.2$ Hz), 6.49 (1H, d, H-2, $J = 1.6$ Hz), 7.11 (2H, d, H-3″ and H-5″, $J = 8.0$ Hz), 7.23 (2H, d, H-2″ and H-6″, $J = 8.0$ Hz), 7.27 (2H, d, H-3′ and H-5′, $J = 8.0$ Hz) and 7.58 (2H, d, H-2′ and H-6′, $J = 8.0$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3 (C-3‴), 21.1 (Ar-CH_3), 21.3 (Ar-CH_3), 35.7 (C-4), 43.9 (C-5), 59.3 (C-6), 60.4 (C-2‴), 126.8 (C-2), 159.7 (C-3), 169.8 (C-1‴), 194.7 (C-1), 122.5, 127.9, 129.4, 129.9, 134.8, 136.6, 139.1 and 141.0 (Aromatic carbons). Mass (M^+): 348. Anal. Calculated for $C_{23}H_{24}O_3$: C-79.28; H-6.94%. Observed: C-79.34; H-7.07%.

*3.3.7. 5-(3,4,5-Trimethoxyphenyl)-3-(p-tolyl)-6-carbethoxy-2-cyclohexen-1-one (**7a**)*

White solid. M.P.: 137 °C. Yield: 86%. IR (ATR, cm^{-1}): 1742, 1657. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.95 (3H, t, H-3‴, $J = 6.8$ Hz), 2.32 (3H, s, Ar-CH_3), 2.95 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.02 (1H, dd, H-4eq, $J = 4.8$ and 14.6 Hz), 3.51 (2H, m, H-5 and H-6), 3.71–3.74 (9H, 3s, Ar-OCH_3), 3.90 (2H, q, H-2‴, $J = 7.2$ Hz), 6.49 (1H, d, H-2, $J = 1.6$ Hz), 6.84–7.06 (3H, m, H-2″, H-5″ and H-6″), 7.24 (2H, d, H-3′ and H-5′, $J = 8.0$ Hz), 7.59 (2H, d, H-2′ and H-6′, $J = 8.4$ Hz). ^{13}C NMR ($CDCl_3$): δ 14.4 (C-3‴), 21.3 (Ar-CH_3), 35.8 (C-4), 43.9 (C-5), 55.98 (−OCH_3), 56.01 (−OCH_3), 59.4 (C-6), 60.3 (C-2‴), 126.9 (C-2), 159.7 (C-3), 169.9 (C-1‴), 194.8 (C-1), 112.0, 112.2, 120.0, 129.9, 134.6, 134.9, 140.9, 148.3 and 149.1 (Aromatic carbons). Mass (M^+): 424. Anal. Calculated for $C_{25}H_{28}O_6$: C-70.74; H-6.65%. Observed: C-70.48; H-6.36%.

*3.3.8. 5-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)-6-carbethoxy-2-cyclohexen-1-one (**8a**)*

Brownish white solid. M.P.: 129 °C. Yield: 69%. IR (ATR, cm^{-1}): 1739, 1656. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.98 (3H, t, H-3‴, $J = 6.8$ Hz), 2.96 (1H, ddd, H-4ax, $J = 2.0$, 4.8 and 14.2 Hz), 3.13 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.55 (2H, m, H-5 and H-6), 3.72–3.90 (9H, 3s, Ar-OCH_3), 4.01 (2H, q, H-2‴, $J = 6.8$ Hz), 6.52 (1H, d, H-2, $J = 2.0$ Hz), 6.86–6.90 (2H, m, H-5″ and H-6″), 6.98 (2H, d, H-3′ and H-5′, $J = 8.8$ Hz), 7.06 (1H, d, H-2″, $J = 1.8$ Hz) and 7.69 (2H, d, H-2′ and H-6′, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3 (C-3‴), 36.3 (C-4), 43.9 (C-5), 54.8 (−OCH_3), 55.8 (−OCH_3), 56.0 (−OCH_3), 59.4 (C-6), 60.3 (C-2‴), 127.3 (C-2), 161.7 (C-3), 170.0 (C-1‴), 194.1 (C-1), 111.9, 112.2, 114.6, 120.0, 121.1, 129.7, 134.3, 148.2, 148.9 and 159.2 (Aromatic carbons). Mass (M^+): 410. Anal. Calculated for $C_{24}H_{26}O_6$: C-70.23; H-6.38%. Observed: C-70.04; H-6.12%.

*3.3.9. 5-Benzo[1,3]dioxol-5-yl-3-(4-nitrophenyl)-6-carbethoxy-2-cyclohexen-1-one (**9a**)*

Pale yellow solid. M.P.: 162 °C. Yield: 62%. IR (ATR, cm^{-1}): 1755, 1641. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.94 (3H, t, H-3‴, $J = 6.9$ Hz), 2.95 (1H, ddd, H-4ax, $J = 2.0$, 4.8 and 14.2 Hz), 3.08 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.65 (2H, m, H-5 and H-6), 4.05 (2H, q, H-2‴, $J = 6.9$ Hz), 5.97 (2H, s, O–CH_2–O), 6.64 (1H, d, H-2, $J = 2.0$ Hz), 6.84–7.07 (3H, m, H-2″, H-5″ and H-6″), 7.94 (2H, d, H-2′ and H-6′, $J = 8.6$ Hz) and 8.22 (2H, d, H-3′ and H-5′, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3 (C-3‴), 35.8 (C-4), 43.9 (C-5), 59.4 (C-6), 60.5 (C-2‴), 101.3 (−O–CH_2–O−), 128.4 (C-2), 157.5 (C-3), 169.5 (C-1‴), 194.8 (C-1), 108.3, 108.5, 121.4, 124.2, 125.8, 135.6, 144.3, 146.6, 147.6 and 148.6 (Aromatic carbons). Mass (M^+): 409. Anal. Calculated for $C_{22}H_{19}NO_7$: C-64.54; H-4.68; N-3.42%. Observed: C-64.03; H-4.14; N-3.26%.

*3.3.10. 3-Benzo[1,3]dioxol-5-yl-5-(4-methoxyphenyl)-6-carbethoxy-2-cyclohexen-1-one (**10a**)*

Electric white solid. M.P.: 153 °C. Yield: 90%. IR (ATR, cm^{-1}): 1744, 1659. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.93 (3H, t, H-3‴, $J = 7.0$ Hz), 2.98 (1H, ddd, H-4ax, $J = 1.6$, 4.4 and 14.6 Hz), 3.11 (1H, dd, H-4eq, $J = 4.8$ and 14.6 Hz), 3.56 (2H, m, H-5 and H-6), 3.86 (3H, s, Ar-OCH_3), 3.96 (2H, q, H-2‴, $J = 7.0$ Hz), 5.97 (2H, s, O–CH_2–O), 6.52 (1H, d, H-2, 1.6 Hz), 6.81/7.04 (3H, m, H-2′, H-5′ and H-6′), 6.97 (2H, d, H-3″ and H-5″, $J = 8.8$ Hz) and 7.68 (2H, d, H-2″ and H-5″, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4 (C-3‴), 35.6 (C-4), 44.0 (C-5), 55.3 (−OCH_3), 59.3 (C-6), 60.4 (C-2‴), 101.3 (−O–CH_2–O−), 129.3 (C-2), 159.2 (C-3), 169.8 (C-1‴), 194.6 (C-1), 108.3, 108.5, 114.7, 121.40, 121.44, 123.7, 136.0, 146.5, 147.6 and 161.7 (Aromatic carbons). Mass (M^+): 394. Anal. Calculated for $C_{23}H_{22}O_6$: C-70.04; H-5.62%. Observed: C-70.44; H-6.01%.

*3.3.11. 3-(4-Chlorophenyl)-5-(4-methoxyphenyl)-6-carbethoxy-2-cyclohexen-1-one (**11a**)*

White solid. M.P.: 138 °C. Yield: 81%. IR (ATR, cm^{-1}): 1747, 1651. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.92 (3H, t, H-3‴, $J = 6.8$ Hz), 2.91 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.02 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.52 (2H, m, H-5 and H-6), 3.72 (3H, s, Ar-OCH_3), 3.88 (2H, q, H-2‴, $J = 7.2$ Hz), 6.54 (1H, d, H-2, $J = 1.6$ Hz), 6.87 (2H, d, H-3″ and H-5″, $J = 6.8$ Hz), 7.30 (2H, d, H-3′ and H-5′, $J = 8.8$ Hz), 7.48 (2H, d, H-2″ and H-5″, $J = 6.8$ Hz) and 7.72 (2H, d, H-2′ and H-6′, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3 (C-3‴), 35.8 (C-4), 43.5 (C-5), 55.5 (−OCH_3), 59.5 (C-6), 60.4 (C-2‴), 128.7 (C-2), 158.7 (C-3), 169.7 (C-1‴), 194.8 (C-1), 114.2, 129.1, 129.3, 133.8, 135.6, 136.7 and 158.5 (Aromatic carbons). Mass (M^+): 384. Anal. Calculated for $C_{22}H_{21}ClO_4$: C-68.66; H-5.50%. Observed: C-69.24; H-5.12%.

*3.3.12. 3-(3,4-Dichlorophenyl)-5-(4-methoxyphenyl)-6-carbethoxy-2-cyclohexen-1-one (**12a**)*

White solid. M.P.: 145 °C. Yield: 69%. IR (ATR, cm^{-1}): 1744, 1660. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.93 (3H, t, H-3‴, $J = 6.7$ Hz), 2.50 (1H, ddd, H-4ax, $J = 2.0$, 4.8 and 14.2 Hz), 3.01 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.64 (2H, m, H-5 and H-6), 3.84 (3H, s, Ar-OCH_3), 3.94 (2H, q, H-2‴, $J = 6.7$ Hz), 6.67 (1H, d, H-2, $J = 2.0$ Hz), 7.01 (2H, d, H-3″ and H-5″, $J = 8.8$ Hz), 7.24 (2H, m, H-5′ and H-6′) and 7.38–7.67 (3H, m, H-′, H-2″ and H-6″). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2 (C-3‴), 37.9 (C-4), 44.0 (C-5), 55.4 (−OCH_3), 59.8 (C-6), 60.3 (C-2‴), 128.2 (C-2), 158.7 (C-3), 169.6 (C-1‴), 194.6 (C-1), 114.3, 125.9, 128.9, 129.8, 131.0, 131.7, 133.2, 134.6, 137.5 and 160.0 (Aromatic carbons). Mass (M^+): 418. Anal. Calculated for $C_{22}H_{20}Cl_2O_4$: C-63.02; H-4.81%. Observed: C-63.56; H-4.23%.

*3.3.13. 3-(3,4-Dimethoxyphenyl)-5-(4-methoxyphenyl) -6-carbethoxy-2-cyclohexen-1-one (**13a**)*

White solid. M.P.: 161 °C. Yield: 91%. IR (ATR, cm^{-1}): 1745, 1663. ^1H NMR ($CDCl_3$): δ 0.95 (3H, t, H-3‴, $J = 7.0$ Hz), 2.79 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.01 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.54 (2H, m, H-5 and H-6), 3.73–3.81 (9H, 3s, Ar-OCH_3), 3.98 (2H, q, H-2‴, $J = 6.9$ Hz), 6.51 (1H, d, H-2, $J = 1.6$ Hz), 6.88–7.06 (5H, m, H-2′, H-5′, H-6′, H-3″ and H-5″) and 7.43 (2H, d, H-2″ and H-6″, $J = 8.4$ Hz). ^{13}C NMR ($CDCl_3$): δ 14.2 (C-3‴), 35.6 (C-4), 43.5 (C-5), 55.4 (−OCH_3), 55.9 (−OCH_3), 59.6 (C-6), 60.6 (C-2‴), 127.0 (C-2), 159.9 (C-3), 170.0 (C-1‴), 194.9 (C-1), 109.8, 111.9, 114.2, 120.4, 121.6, 129.9, 133.8, 134.5, 149.1, 151.4 and 158.6 (Aromatic carbons). Mass (M^+): 410. Anal. Calculated for $C_{24}H_{26}O_6$: C-70.23; H-6.38%. Observed: C-70.54; H-6.49%.

*3.3.14. 3-(4-Fluorophenyl)-5-(3-nitrophenyl)-6-carbethoxy-2-cyclohexen-1-one (**14a**)*

White solid. M.P.: 134 °C. Yield: 72%. IR (ATR, cm^{-1}): 1739, 1661. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.86 (3H, t, H-3‴, $J = 7.2$ Hz), 2.96–3.11 (2H, m, H-4eq and H-4ax), 3.58 (2H, m, H-5 and H-6), 4.01 (2H, q, H-2‴, $J = 7.2$ Hz), 6.51 (1H, d, H-2, $J = 2.0$ Hz), 7.21–7.43 (4H, m, H-2′, H-3′, H-5′ and H-6′) and 7.58–7.72 (4H, m, H-2″, H-4″, H-5″ and H-6″). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C-3‴), 34.4 (C-4), 42.2 (C-5), 57.9 (C-6), 60.8 (C-2‴), 128.1 (C-2), 158.3 (C-3), 169.4 (C-1‴), 194.7 (C-1), 116.2, 123.1, 129.3, 130.0, 133.2, 138.5, 162.6 and 165.1 (Aromatic carbons). Mass (M^+): 383. Anal. Calculated for $C_{21}H_{18}FNO_5$: C-65.79; H-4.73; N-3.65%. Observed: C-65.27; H-4.23; N-3.26%.

*3.3.15. 3-(4-Fluorophenyl)-5-phenyl-6-carbethoxy-2-cyclohexen-1-one (**15a**)*

Greenish white solid. M.P.: 178 °C. Yield: 74%. IR (ATR, cm^{-1}): 1733, 1659. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.89 (3H, t, H-3‴, $J = 7.2$ Hz), 2.93 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.02 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.53 (2H, m, H-5 and H-6), 3.95 (2H, q, H-2‴, $J = 7.2$ Hz), 6.49 (1H, d, H-2, $J = 1.6$ Hz), 7.20–7.37 (7H, m, H-2″-6″, H-3′ and H-5′) and 7.69–7.73 (2H, m, H-2′ and H-6′). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1 (C-3‴), 35.6 (C-4), 44.2 (C-5), 59.2 (C-6), 60.7 (C-2‴), 159.0 (C-3), 169.9 (C-1‴), 195.0 (C-1), 127.1 (C-2), 116.1, 123.1, 127.9, 128.9, 129.1, 134.2, 143.6 and 162.6 (Aromatic carbons). Mass (M^+): 338. Anal. Calculated for $C_{21}H_{19}FO_3$: C-74.54; H-5.66%. Observed: C-74.12; H-5.16%.

*3.3.16. 3,5-(Diphenyl)-6-carbethoxy-2-cyclohexen-1-one (**16a**)*

White solid. M.P.: 155 °C. Yield: 95%. IR (ATR, cm^{-1}): 1734, 1652. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.04 (3H, t, H3‴, $J = 6.8$ Hz), 2.95 (1H, ddd, H-4ax, $J = 1.6$, 4.8 and 14.2 Hz), 3.06 (1H, dd, H-4eq, $J = 4.8$ and 14.2 Hz), 3.80 (2H, m, H-5 and H-6), 4.04 (2H, q, H-2‴, $J = 7.2$ Hz), 6.57 (1H, d, H-2, $J = 2.0$ Hz), 7.27–7.57 and (10H, m, H-2″-6″ and H-2′-6′). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.9 (C-3‴), 36.1 (C-4), 44.1 (C-5), 59.6 (C-6), 60.9 (C-2‴), 124.1 (C-2), 158.5 (C-3), 169.2 (C-1‴), 194.0 (C-1), 126.2, 127.3, 127.5, 128.8, 128.9, 130.5, 137.7 and 141.0 (Aromatic carbons). Mass (M^+): 320. Anal. Calculated for $C_{21}H_{20}O_3$: C-78.73; H-6.29%. Observed: C-79.14; H-6.38%.

*3.4. General procedure for the synthesis of 2H-indazol-3-ols (**1b**–**16b**)*

To a mixture of cyclohexenone (1 mmol) and glacial acetic acid (1.5 mL) in ethanol (1.5 mL) was added hydrazine hydrate (2 mmol). The mixture was then placed in the center of a house-hold microwave oven, beside a beaker containing 50 g ice, and irradiated for 3 min in total with 30 s pulse and cooling in between. After irradiation, ice cold distilled water (20 mL) was added to the reaction mixture. This aq. suspension was then centrifuged and supernatant was discarded. Precipitate collected was washed thrice, using centrifugation, with distilled water (20 mL) to remove acetic acid. The wet solid was lyophilized to get 98% pure powdery solid of 2H-indazol-3-ols (**1b**–**16b**). Further purification, if required, was done by washing it with cold ethanol. All the products were characterized by IR, NMR and mass spectra.

*3.4.1. 4,5-Dihydro-4-(3,4-dimethoxyphenyl)-6-phenyl-2H-indazol-3-ol (**1b**)*

White solid. M.P.: 168 °C. Yield: 83%. IR (ATR, cm^{-1}): 3321, 3212. ^1H NMR (DMSO-d_6, 400 MHz): δ 2.81 (1H, dd, H-5eq, $J = 3.4$ and 17.2 Hz), 3.09 (1H, ddd, H-5ax, $J = 2.4$, 8.2 and 17.2 Hz), 3.85 & 3.86 (6H, 2s, Ar-OCH_3), 4.07 (1H, dd, 4-H, $J = 3.4$ and 8.2 Hz), 6.61 (1H, d, H-7, $J = 2.4$ Hz), 6.80–6.87 (3H, m, H-2″, H-5″ and H-6″), 7.18–7.35 (5H, m, H-2′-6′) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 33.2 (C-4), 36.8 (C-5), 55.1 (−OCH_3), 55.4 (−OCH_3), 98.6 (C-3), 113.6 (C-7), 136.1 (C-3a), 139.3 (C-7a), 156.8 (C-6), 111.4, 122.2, 125.5, 128.0, 128.9, 129.2, 133.5, 145.2, 149.3 and 150.1 (Aromatic carbons). Mass (M^+): 348. Anal. Calculated for $C_{21}H_{20}N_2O_3$: C-72.40; H-5.79; N-8.04%. Observed: C-72.44; H-6.05; N-8.26%.

*3.4.2. 4,5-Dihydro-6-phenyl-4-p-tolyl-2H-indazol-3-ol (**2b**)*

White solid. M.P.: 227 °C. Yield: 73%. IR (ATR, cm^{-1}): 3318, 3204. ^1H NMR (DMSO-d_6, 400 MHz): δ 2.28 (3H, s, Ar-CH_3), 2.81 (1H, dd, H-5eq, $J = 3.6$ and 17.2 Hz), 3.14 (1H, ddd, H-5ax, $J = 2.4$, 8.6 and 17.2 Hz), 4.09 (1H, dd, 4-H, $J = 3.6$ and 8.6 Hz), 6.67 (1H, d, H-7, $J = 2.4$ Hz), 7.08 (2H, d, H-2″ and H-6″, $J = 7.8$ Hz), 7.29–7.54 (7H, m, H-2′-6′, H-3″ and H-5″) and 9.73 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 21.2 (Ar-CH_3), 33.4 (C-4), 36.7 (C-5), 98.5 (C-3), 114.2 (C-7), 136.3 (C-3a), 139.4 (C-7a), 156.4 (C-6), 125.8, 127.9, 128.6, 129.3, 129.7, 134.5, 138.7 and 144.3 (Aromatic carbons). Mass (M^+): 302. Anal. Calculated for $C_{20}H_{18}N_2O$: C-79.44; H-6.00; N-9.26%. Observed: C-79.03; H-6.53; N-9.46%.

*3.4.3. 4,5-Dihydro-4-(4-methoxyphenyl)-6-phenyl-2H-indazol-3-ol (**3b**)*

Brownish white solid. M.P.: 232 °C. Yield: 81%. IR (ATR, cm^{-1}): 3308, 3210. ^1H NMR (DMSO-d_6, 400 MHz): δ 2.79 (1H, dd, H-5eq,

J = 3.6 and 17.2 Hz), 3.00 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.2 Hz), 3.64 (3H, s, Ar-OCH_3), 4.10 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 6.68 (1H, d, H-7, J = 2.4 Hz), 6.72–7.38 (9H, m, Aromatic protons) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 33.8 (C-4), 36.7 (C-5), 55.3 (−OCH_3), 98.4 (C-3), 113.9 (C-7), 136.6 (C-3a), 137.8 (C-7a), 156.4 (C-6), 125.4, 126.0, 128.2, 129.60, 129.63, 129.8, 137.3 and 157.9 (Aromatic carbons). Mass (M^+): 318. Anal. Calculated for $C_{20}H_{18}N_2O_2$: C-75.45; H-5.70; N-8.80%. Observed: C-75.07; H-6.09; N-9.16%.

3.4.4. 4,5-Dihydro-4-(3,4,5-trimethoxyphenyl)-6-phenyl-2H-indazol-3-ol (**4b**)

White solid. M.P.: 179 °C. Yield: 86%. IR (ATR, cm^{-1}): 3319, 3216. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.81 (1H, dd, H-5eq, J = 3.4 and 16.8 Hz), 3.08 (1H, ddd, H-5ax, J = 2.4, 8.6 and 16.8 Hz), 3.88–3.97 (9H, 3s, Ar-OCH_3), 4.09 (1H, dd, 4-H, J = 3.4 and 8.6 Hz), 6.54 (1H, d, H-7, J = 2.4 Hz), 6.67 (2H, m, H-2″ and H-6″), 7.08–7.35 (5H, m, H-2′-6′) and 9.72 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 33.9 (C-4), 36.5 (C-5), 55.7 (−OCH_3), 55.9 (−OCH_3), 98.3 (C-3), 113.4 (C-7), 137.5 (C-3a), 138.2 (C-7a), 156.4 (C-6), 111.9, 118.9, 125.9, 129.7, 132.0, 134.5, 147.4 and 148.7 (Aromatic carbons). Mass (M^+): 378. Anal. Calculated for $C_{22}H_{22}N_2O_4$: C-69.83; H-5.86; N-7.40%. Observed: C-70.29; H-6.15; N-7.26%.

3.4.5. 4,5-Dihydro-4-(3,4-dimethoxyphenyl)-6-p-tolyl-2H-indazol-3-ol (**5b**)

White solid. M.P.: 193 °C. Yield: 81%. IR (ATR, cm^{-1}): 3321, 3215. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.37 (3H, s, Ar-CH_3), 2.71 (1H, dd, H-5eq, J = 3.4 and 17.2 Hz), 3.11 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.2 Hz), 3.81 & 3.85 (6H, 2s, Ar-OCH_3), 4.14 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 6.67 (1H, d, H-7, J = 2.4 Hz), 6.77–6.89 (3H, m, H-2″, H-5″ and H-6″), 7.19–7.24 (2H, m, H-3′ and H-5′), 7.31 (2H, d, H-2′ and H-6, J = 8 Hz) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 21.2 (Ar-CH_3), 33.6 (C-4), 36.7 (C-5), 55.0 (−OCH_3), 55.2 (−OCH_3), 98.6 (C-3), 112.9 (C-7), 136.4 (C-3a), 148.1 (C-7a), 156.9 (C-6), 111.3, 121.2, 122.4, 125.6, 128.9, 135.2, 136.1, 137.6, 150.3 and 151.1 (Aromatic carbons). Mass (M^+): 362. Anal. Calculated for $C_{22}H_{22}N_2O_3$: C-72.91; H-6.12; N-7.73%. Observed: C-72.34; H-6.28; N-7.31%.

3.4.6. 4,5-Dihydro-4,6-di-p-tolyl-2H-indazol-3-ol (**6b**)

White solid. M.P.: 211 °C. Yield: 79%. IR (ATR, cm^{-1}): 3321, 3210. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.26 & 2.31 (6H, 2s, Ar-CH_3), 2.60 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 2.72 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.2 Hz), 4.01 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 6.71 (1H, d, H-7, J = 2.4 Hz), 6.96–7.38 (4H, m, H-2″, H-3″, H-5″ and H-6″), 7.54 (2H, d, H-3′ and H-5′, J = 8.0 Hz), 7.60 (2H, d, H-2′ and H-6′, J = 8.0 Hz) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6): δ 21.1 (Ar-CH_3), 21.2 (Ar-CH_3), 33.7 (C-4), 36.5 (C-5), 98.4 (C-3), 114.0 (C-7), 136.9 (C-3a), 140.5 (C-7a), 156.9 (C-6), 125.9, 127.3, 127.5, 129.2, 129.3, 135.6, 136.1, 136.4 and 141.2 (Aromatic carbons). Mass (M^+): 316. Anal. Calculated for $C_{21}H_{20}N_2O$: C-79.72; H-6.37; N-8.85%. Observed: C-79.44; H-6.49; N-8.56%.

3.4.7. 4,5-Dihydro-4-(3,4,5-trimethoxyphenyl)-6-p-tolyl-2H-indazol-3-ol (**7b**)

White solid. M.P.: 181 °C. Yield: 78%. IR (ATR, cm^{-1}): 3312, 3211. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.28 (3H, s, Ar-CH_3), 2.81 (1H, dd, H-5eq, J = 3.4 and 16.8 Hz), 3.09 (1H, ddd, H-5ax, J = 2.4, 8.6 and 16.8 Hz), 3.88–3.97 (9H, 3s, Ar-OCH_3), 4.09 (1H, dd, 4-H, J = 3.4 and 8.6 Hz), 6.54 (1H, d, H-7, J = 2.4 Hz), 6.69–6.79 (2H, m, H-2″ and H-6″), 7.11 (2H, d, H-3′ and H-5′, J = 8.0 Hz), 7.32 (2H, d, H-2′ and H-6′, J = 8.0 Hz) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 21.1 (Ar-CH_3), 33.9 (C-4), 36.5 (C-5), 55.7 (−OCH_3), 55.9 (−OCH_3), 98.3 (C-3), 111.4 (C-7), 134.5 (C-3a), 137.5 (C-7a), 156.3 (C-6), 111.9, 118.9, 125.9, 129.7, 132.0, 138.2, 147.4 and 148.7 (Aromatic carbons). Mass (M^+): 392. Anal. Calculated for $C_{23}H_{24}N_2O_4$: C-70.39; H-6.16; N-7.14%. Observed: C-70.68; H-5.87; N-7.38%.

3.4.8. 4,5-Dihydro-4-(3,4-dimethoxyphenyl)-6-(4-methoxyphenyl)-2H-indazol-3-ol (**8b**)

Brownish white solid. M.P.: 186 °C. Yield: 69%. IR (ATR, cm^{-1}): 3318, 3217. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.88 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 3.06 (1H, ddd, H-5ax, J = 2.4, 8.8 and 17.6 Hz), 3.63–3.73 (9H, 3s, Ar-OCH_3), 4.08 (1H, dd, 4-H, J = 3.6 and 8.8 Hz), 6.54 (1H, dd, H-6″, J = 2.0 and 8.4 Hz), 6.62 (1H, d, H-7, J = 2.4), 6.72 (1H, d, H-5″, J = 8.4 Hz), 6.82 (1H, d, H-2″, J = 2.0 Hz), 6.89 (2H, d, H-3′ and H-5′, J = 6.8 Hz), 7.40 (2H, d, H-2′ and H-6′, J = 6.8 Hz) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.3 (C-4), 36.6 (C-5), 55.6 (−OCH_3), 55.8 (−OCH_3), 56.0 (−OCH_3), 98.4 (C-3), 112.1 (C-7), 133.1 (C-3a), 136.6 (C-7a), 156.3 (C-6), 111.7, 114.4, 118.9, 126.8, 127.1, 127.6, 138.4, 147.5, 148.8 and 159.3 (Aromatic carbons). Mass (M^+): 378. Anal. Calculated for $C_{22}H_{22}N_2O_4$: C-69.83; H-5.86; N-7.40%. Observed: C-69.43; H-6.17; N-7.29%.

3.4.9. 4-(Benzo[d][1,3]dioxol-5-yl)-4,5-dihydro-6-(4-nitrophenyl)-2H-indazol-3-ol (**9b**)

Pale yellow solid. M.P.: 198 °C. Yield: 82%. IR (ATR, cm^{-1}): 3324, 3221. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.84 (1H, dd, H-5eq, J = 3.8 and 17.4 Hz), 3.14 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.4 Hz), 4.13 (1H, dd, 4-H, J = 3.8 and 8.6 Hz), 5.85 (2H, s, O–CH_2–O), 6.53 (1H, dd, H-6″, J = 1.6 and 8.0 Hz), 6.62 (1H, d, H-2″, J = 1.6), 7.01 (1H, d, H-7, J = 2.4 Hz), 7.12 (2H, d, H-2′ and H-6′, J = 8.8 Hz), 8.14 (2H, d, H-2′ and H-6′, J = 8.8 Hz) and 9.69 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.1 (C-4), 36.4 (C-5), 99.3 (C-3), 101.0 (–O–CH_2–O–), 108.3 (C-7), 136.1 (C-3a), 139.4 (C-7a), 156.8 (C-6), 107.8, 120.1, 124.3, 126.5, 134.6, 141.7, 145.8, 146.5, 147.1 and 147.4 (Aromatic carbons). Mass (M^+): 377. Anal. Calculated for $C_{20}H_{15}N_3O_5$: C-63.66; H-4.01; N-11.14%. Observed: C-63.14; H-4.09; N-10.39%.

3.4.10. 6-(Benzo[d][1,3]dioxol-5-yl)-4,5-dihydro-4-(4-methoxyphenyl)-2H-indazol-3-ol (**10b**)

White solid. M.P.: 203 °C. Yield: 89%. IR (ATR, cm^{-1}): 3307, 3198. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.80 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 3.02 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.2 Hz), 3.88 (3H, s, Ar-OCH_3), 4.08 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 5.85 (2H, s, O–CH_2–O), 6.54 (1H, dd, H-6′, J = 1.60 and 8.0 Hz), 6.62 (1H, d, H-2′, J = 1.60 Hz), 6.64 (1H, d, H-7, J = 2.4), 6.68 (1H, d, H-5′, J = 8.0 Hz), 6.87 (2H, d, H-3″ and H-5″, J = 8.8 Hz), 7.39 (2H, d, H-2″ and H-6″, J = 8.8 Hz) and 9.73 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.1 (C-4), 36.6 (C-5), 55.6 (−OCH_3), 98.7 (C-3), 101.0 (–O–CH_2–O–), 107.8 (C-7), 136.6 (C-3a), 139.8 (C-7a), 156.2 (C-6), 108.2, 114.4, 120.0, 126.8, 132.6, 132.8, 145.7, 147.3, 148.0, and 159.3 (Aromatic carbons). Mass (M^+): 362. Anal. Calculated for $C_{21}H_{18}N_2O_4$: C-69.60; H-5.01; N-7.73%. Observed: C-69.41; H-5.58; N-7.16%.

3.4.11. 6-(4-Chlorophenyl)-4,5-dihydro-4-(4-methoxyphenyl)-2H-indazol-3-ol (**11b**)

Greenish white solid. M.P.: 169 °C. Yield: 87%. IR (ATR, cm^{-1}): 3315, 3191. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.76 (1H, dd, H-5eq, J = 3.6 and 16.8 Hz), 3.06 (1H, ddd, H-5ax, J = 2.4, 8.6 and 16.8 Hz), 3.89 (3H, s, Ar-OCH_3), 4.03 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 6.71 (2H, d, H-3″ and H-5″, J = 8.8 Hz), 6.77 (1H, d, H-7, J = 2.4 Hz), 6.98 (2H, d, H-2″ and H-6″, J = 8.8 Hz), 7.34 (2H, d, H-3′ and H-5′, J = 8.8 Hz), 7.45 (2H, d, H-2′ and H-6′, J = 8.8 Hz) and 9.68 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 33.5 (C-4), 36.6 (C-5), 55.4 (−OCH_3), 99.1 (C-3), 113.9 (C-7), 135.5 (C-3a), 139.4 (C-7a), 156.3 (C-6), 127.3, 128.2. 128.9, 129.3, 132.4, 134.5, 144.5, and 157.9 (Aromatic carbons).

Mass (M^+): 352. Anal. Calculated for $C_{20}H_{17}ClN_2O_2$: C-68.09; H-4.86; N-7.94%. Observed: C-67.92; H-4.91; N-7.26%.

*3.4.12. 6-(3,4-Dichlorophenyl)-4,5-dihydro-4-(4-methoxyphenyl)-2H-indazol-3-ol (**12b**)*

Greenish white solid. M.P.: 173 °C. Yield: 71%. IR (ATR, cm^{-1}): 3318, 3209. ^{1}H NMR (DMSO-d_6): δ 2.54 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 3.07 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.2 Hz), 3.78 (3H, s, Ar-OCH_3), 4.07 (1H, dd, 4-H, J = 3.6 and 8.6 Hz), 6.44 (1H, d, H-7, J = 2.4), 6.73 (2H, d, H-3″ and H-5″, J = 8.8 Hz), 6.99 (2H, d, H-2″ and H-6″, J = 8.8 Hz), 7.16 (1H, d, H-5′, J = 8.4 Hz), 7.33 (1H, dd, H-6′, J = 1.0 and 8.4 Hz), 7.51 (1H, d, H-2′, J = 1.0 Hz) and 9.75 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.0 (C-4), 37.1 (C-5), 55.4 (-OCH_3), 98.2 (C-3), 113.8 (C-7), 137.0 (C-3a), 139.9 (C-7a), 156.7 (C-6), 127.9, 128.5, 129.6, 130.3, 131.7, 132.6, 133.1, 133.4, 145.1, and 158.0 (Aromatic carbons). Mass (M^+): 386. Anal. Calculated for $C_{20}H_{16}Cl_2N_2O_2$: C-62.03; H-4.16; N-7.23%. Observed: C-61.76; H-5.01; N-7.21%.

*3.4.13. 4,5-Dihydro-6-(3,4-dimethoxyphenyl)-4-(4-methoxyphenyl)-2H-indazol-3-ol (**13b**)*

White solid. M.P.: 192 °C. Yield: 90%. IR (ATR, cm^{-1}): 3324, 3217. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.79 (1H, dd, H-5eq, J = 3.2 and 16.8 Hz), 3.13 (1H, ddd, H-5ax, J = 2.4, 8.6 and 16.8 Hz), 3.73–3.79 (9H, 3s, Ar-OCH_3), 4.09 (1H, dd, 4-H, J = 3.2 and 8.6 Hz), 6.56 (1H, d, H-7, J = 2.4), 6.83 (1H, d, H-5′, J = 8.8 Hz), 6.94 (2H, d, H-3″ and H-5″, J = 8.8 Hz), 7.24 (1H, d, H-2′, J = 2.2 Hz), 7.29 (1H, dd, H-6′, J = 2.2 and 8.8 Hz), 7.31 (2H, d, H-2″ and H-6″, J = 8.8 Hz) and 9.73 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.4 (C-4), 36.9 (C-5), 55.5 (−OCH_3), 55.9 (−OCH_3), 56.1 (−OCH_3), 98.6 (C-3), 112.2 (C-7), 136.5 (C-3a), 138.4 (C-7a), 156.4 (C-6), 111.4, 114.3, 119.0, 126.4, 127.3. 127.7, 133.2, 148.3, 148.8, and 158.2 (Aromatic carbons). Mass (M^+): 378. Anal. Calculated for $C_{22}H_{22}N_2O_4$: C-69.83; H-5.89; N-7.40%. Observed: C-69.64; H-6.03; N-7.82%.

*3.4.14. 6-(4-Fluorophenyl)-4,5-dihydro-4-(3-nitrophenyl)-2H-indazol-3-ol (**14b**)*

White solid. M.P.: 169 °C. Yield: 89%. IR (ATR, cm^{-1}): 3305, 3201. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.72 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 3.15 (1H, ddd, H-5ax, J = 2.4, 8.4 and 17.2 Hz), 4.21 (1H, dd, 4-H, J = 3.2 and 8.4 Hz), 6.75 (1H, d, H-7, J = 2.4), 6.79 (2H, d, H-3′ and H-5′, J = 7.2 Hz), 7.08–7.15 (4H, m, H-2′, H-6′, H-5″ and H-6″), 7.37–7.41 (2H, m, H-2″ and H-4″) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 31.5 (C-4), 35.3 (C-5), 97.3 (C-3), 115.7 (C-7), 136.9 (C-3a), 141.6 (C-7a), 155.7 (C-6), 115.9, 125.5, 127.3, 127.4, 128.4, 129.9, 132.4, 135.5, 160.8 and 162.4 (Aromatic carbons). Mass (M^+): 351. Anal. Calculated for $C_{19}H_{14}FN_3O_3$: C-64.95; H-4.02; N-11.61%. Observed: C-65.17; H-4.61; N-11.03%.

*3.4.15. 6-(4-Fluorophenyl)-4,5-dihydro-4-phenyl-2H-indazol-3-ol (**15b**)*

Pale white solid. M.P.: 220 °C. Yield: 84%. IR (ATR, cm^{-1}): 3311, 3209. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.80 (1H, dd, H-5eq, J = 3.6 and 17.2 Hz), 3.11 (1H, ddd, H-5ax, J = 2.4, 8.6 and 17.4 Hz), 4.17 (1H, dd, H-4, J = 3.6 and 8.6 Hz), 6.72 (1H, d, H-7, J = 2.4), 7.07–7.18 (7H, m, H-3′, H-5′, H-2″,-6″), 7.46 (2H, d, H-2′ and H-6′, J = 8.4 Hz) and 9.70 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.3 (C-4), 36.6 (C-5), 98.3 (C-3), 115.7 (C-7), 136.9 (C-3a), 140.3 (C-7a), 157.2 (C-6), 125.9, 126.5, 127.4, 128.6, 132.0, 141.7, 145.5, and 161.4 (Aromatic carbons). Mass (M^+): 306. Anal. Calculated for $C_{19}H_{15}FN_2O$: C-74.5; H-4.94; N-9.14%. Observed: C-74.32; H-5.35; N-9.26%.

*3.4.16. 4,5-Dihydro-4,6-diphenyl-2H-indazol-3-ol (**16b**)*

White solid. M.P.: 215 °C. Yield: 93%. IR (ATR, cm^{-1}): 3321, 3212. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.86 (1H, dd, H-5eq, J = 3.2 and 16.8 Hz), 3.15 (1H, ddd, H-5ax, J = 2.4, 8.4 and 16.6 Hz), 4.16 (1H, dd, 4-H, J = 3.2 and 8.4 Hz), 6.74 (1H, d, H-7, J = 2.4), 7.10–7.46 (10H, m, Aromatic protons) and 9.71 (2H, brs, OH and NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 34.6 (C-4), 36.7 (C-5), 98.7 (C-3), 113.8 (C-7), 136.6 (C-3a), 140.6 (C-7a), 156.8 (C-6), 125.5, 126.3, 127.3, 127.9, 128.5, 129.0, 141.6 and 145.7 (Aromatic carbons). Mass (M+): 288. Anal. Calculated for $C_{19}H_{16}N_2O$: C-79.14; H-5.59; N-9.72%. Observed: C-79.24; H-6.01; N-9.43%.

3.5. In vitro anti-fungal activity (food poisoning method)

Phyto-pathogenic test fungi, *Rhizoctonia solani* ITCC 5563 and *Sclerotium rolfsii* ITCC 6181 were procured from Indian Type Culture Collection (ITCC) center, Division of Plant Pathology, Indian Agricultural Research Institute, New Delhi-110 012, India. Cultures of the test fungi were maintained on Potato Dextrose Agar (PDA) slant at 27 °C for at least 4–7 days and were sub-cultured in Petri dishes prior to testing. The test fungi were routinely grown on fresh slant tubes of PDA and stored at 4 °C.

The above synthesized compounds were tested for their ability to inhibit soil borne pathogenic fungi against the standard fungicide hexaconazole. The fungicidal activity of synthesized compounds was evaluated at various concentrations by the poisoned food technique using PDA (potato dextrose agar) media. The readymade PDA medium (39 g) was suspended in distilled water (1000 mL) and heated to boiling until completely dissolved. The medium and petri dishes were autoclaved at 15 mm Hg for 30 min. These compounds were tested at concentrations of 500, 250, 125, 62.5, 31.25, 15.63, 7.81 and 3.90 μg mL^{-1}. A stock solution of 5000 μg mL^{-1} was prepared in Acetone or DMSO. Acetone or DMSO was used as a control. These solutions were added to the media (50 mL) in conical flasks to obtain the desired concentrations of the test compounds in the media. The medium was poured into a set of two petri dishes (90 cm in diameter) under aseptic conditions in a laminar flow hood. The plates were kept in the laminar flow chamber for solidification of the media. After solidification, a 5 mm (diameter) mycelia plug cut from the actively growing front of a 2 week old colony of the desired pathogenic fungus was then placed with the inoculums side down in the center of each treatment plate, aseptically. Treated petri dishes were then incubated at 27 °C till the fungal growth was almost complete in the control plates. All experiments were in quadruplet for each treatment against each fungus.

3.5.1. Recording of observations

The mycelia growth of fungus (mm) in both treated (T) and control (C) petri dishes was measured diametrically. The mean and standard errors were calculated from the four replicates of each treatment and the percentage inhibition of growth (I) was calculated using the following formula

$$\text{Inhibition } (\%I) : (C - T) \times 100/C$$

3.5.2. Calculation of LC_{50} values

For calculation of LC_{50} values (lethal concentration for 50% inhibition; μg mL^{-1}), the percent inhibition was converted to corrected percent inhibition by using Abbott's formula:

$$\text{Corrected inhibition } (\%) : (I - \text{CF}) \times 100/(100 - \text{CF})$$

where CF is the correction factor obtained by the equation:

$$\text{Correction factor } (\text{CF}) : (9 - C) \times 100/C$$

where 9 is the diameter of the petri dish in cm and C is the diameter of growth of the fungus in control plates. From the concentration (μg mL^{-1}) and corresponding corrected percentage inhibition data

of each compound, the LC_{50} (μg mL^{-1}) values were calculated statistically by computer programme (Indostat Services, Hyderabad) on a personal computer.

3.6. In vitro anti-bacterial activity (disk diffusion method)

Two phytopathgenic bacteria *Xanthomonas oryzae* ITCC B-47 and *Erwinia crysanthemi* ITCC B-40 were procured from Indian Type Culture Collection (ITCC) center, Division of Plant Pathology, Indian Agricultural Research Institute, New Delhi-110 012, India. Two beneficial bacteria *Bacillus thuringiensis* MTCC 6941 and *Bacillus pumilis* MTCC 2466 and three human pathogens *Staphylococcus aureus* MTCC 3160, *Pseudomonas aeruginosa* MTCC 2581 and *Klebsiella pneumoneae* MTCC 7028 were procured from Microbial Type Culture Collection and gene bank, Institute of Microbial Technology, sector-39A, Chandigarh 110 036, India. Cultures of the test bacteria were maintained on nutrient Agar (NA) slant at 37 °C for 1–3 days, depending upon the growth period of bacteria, and were subcultured in nutrient broath culture tubes prior to testing. The test bacteria were routinely grown on fresh slant tubes of NA and stored at 4 °C.

All the synthesized compounds were tested for their ability to inhibit above mentioned bacteria against the standard antibiotics Streptomycin, Ampicillin and Kanamycin. The concentrations of the latter were used as recommended manufacturer. The anti-bacterial activity of synthesized compounds was evaluated at single concentration (100 μg/disc) by disk diffusion technique using NA (Nutrient agar) media. The readymade NA medium (37 g) was suspended in distilled water (1000 mL) and heated to boiling until completely dissolved. The medium and petri dishes were autoclaved at 15 mm Hg for 30 min. A stock solution of 20,000 μg mL^{-1} for all the compounds was prepared in DMSO. DMSO (5 μL) was used as control. The medium (25 mL) was poured into petri dishes (90 cm in diameter) under aseptic conditions in a laminar flow hood. The plates were kept in the laminar flow chamber for solidification of the media. After solidification 100 μL of fresh culture (log phase) was spread on the surface of solidified medium with the help of a spreader. The plates were then kept in laminar flow for drying. Once dried five plain sterile disks were placed in the plate and 5 μL of stock solution was loaded on each disk. Different compound was loaded on different disk. In control plate commercially procured antibiotics (25 μg/disk) and DMSO (5 μL) was loaded. Plates were then kept at 37 °C. After 24 h plates were taken out from incubator and zone of inhibition (in mm) was recorded for all the compounds tested and commercial antibiotics. Zone of inhibition for synthesized compounds were reported relative to zone of inhibition of known antibiotics. All experiments were in quadruplet for each treatment against each bacteria.

Minimum Inhibitory Concentration (MIC) was calculated using a method reported in literature [50].

3.7. Anti-oxidant activity (DPPH UV–Vis assay)

Anti-oxidant activity of synthesized compounds was checked using DPPH UV–Vis assay [51]. A stock solution of 10 mg mL^{-1} for all the compounds was prepared in DMSO. First all the compounds were screened for their anti-oxidant activity with 20 μL of stock solution. Compounds with good anti-oxidant activity were then checked at different concentrations (5, 10, 20, 30, 40, 50, 100, 150, 200 and 250 μL of stock solution). Gallic acid (GA) was used as standard. 0.1 mM methanolic solution of DPPH (2,2-diphenyl-1-picrylhydrazyl) was prepared and stored at 4 °C until used. Different compounds (5–250 μL) and GA (100 ppm, 5–250 μL) were added to different test tubes. Five milliliters of 0.1 mM methanolic solution of DPPH was added to these test tubes and the contents were shaken vigorously. The tubes were allowed to stand at room temperature for 20 min in the dark. The control was prepared as above without any compound (only DMSO), and methanol was used for the baseline correction. The absorbance of the samples was measured at 517 nm. Radical scavenging activity was calculated using the following formula:

$$\text{Percent radical scavenging activity} = (\text{Control OD} - \text{sample OD})/\text{Control OD} \times 100.$$

4. Conclusion

We report the green synthesis of chalcone, cyclohexenone and indazole derivatives (sixteen each), using microwave irradiation for activation under solvent less condition, their characterization and bio-efficacy evaluation. Microwave heating, which was used for synthesis, showed several advantages *viz*., solvent less reaction, reduced reaction time (from hours to minutes), increased yield (3–16%) and high purity. Biological activity data showed promising results as the compounds were very selective in nature and results for some compounds are very much comparable with the control/standard used. The microwave method, being very simple and cost effective, can be used for the synthesis of more potent analogues of mentioned compounds that too in large (gram) quantities.

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