SYNTHESIS, SPECTRAL STUDIES, ANTI-OXIDANT, ANTI-INFLAMMATORY AND ANTIBACTERIAL ACTIVITIES OF 3-(1H-INDOL-3-YL)-1-PHENYLPROP-2-EN-1-ONE DERIVATIVES

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ABSTRACT

The 3-(1H-indol-3-yl)-1-phenylprop-2-en-1-one derivatives were synthesized by conventional method. The compounds are analyzed by IR, NMR, mass spectral and anti-oxidant, anti-inflammatory and antimicrobial activities are carried out. The studies identify the active compounds accountable for anti-oxidants and anti-inflammatory. Studies are extremely required for future drug growth.

Keywords: IR, NMR, Anti-oxidant, Anti-inflammatory, Antimicrobial.

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INTRODUCTION

Indole derivatives are very significant heterocyclic compounds that induced several biological activities^{1,2}. Indole derivatives via palladium-catalyzed hetero annulation of alkynes by Amides with ethyl diazoacetate³⁻⁵. *N*-substituted anilines and alkanolamines⁶, 5 α -androsterone-3,17-dione with 1-methyl-1-phenylhydrazine^{7,8}. The grounding of (Z)-16- (7-aza-1H-indol-1-yl) methylene-17-oxoandrosterone-5-en-3 β -yl-acetate by the response of 17-chloro-16-formylandrosterone-5,16-dien-3-yl acetate with 7-azaindole under N₂ atmosphere⁹, Antiallergic¹⁰, anticancer¹¹, anti-inflammatory¹², antimalarial¹³, antitubercular¹⁴, antiviral¹⁵. Indole scaffold have been establishing in several important artificial drug molecules which give a precious plan for treatment and binds with elevated similarity to the multiple receptors helpful in developing novel useful derivatives¹⁶⁻¹⁸.

EXPERIMENTAL

Measurements

IR spectra were recorded in AVATAR-330 FT-IR spectrophotometer. ¹H and ¹³C NMR recorded on BRUKER AMX working at 300 MHz.

Synthesis of 3-(1H-indol-3-yl)-1-phenylprop-2-en-1-one Derivatives

A combination of indole-3-carbaldehyde (1 mmol), substituted acetophenone (1 mmol) and 20 mL of ethanol to be added into a refluxing flask and few grams of sodium methoxide was added and refluxed for 4 hrs at 75 °C and this combination was monitored by TLC (Scheme 1). The final mass was transfer into ice-cold water to the removal of unreacted aldehyde. The residue was obtained and purified by chromatography technique by using benzene: chloroform mixture (8:2) as an eluent.

Anti-Oxidant Studies

DPPH Scavenging Assay

The ability to scavenging the stable free radical, DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) free radical method is an antioxidant assay was measured as a decrease in absorbance at 517 nm by the method.

Procedure

Methanolic solution of DPPH (90.30 mM), an identical volume of ethanolic Rhizome of *Cyperus rotundus* L (250-1500 μ g) was added and prepared up to 1.0 mL with methanol DPPH. The solutions

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were stunned well & made to stand the solutions at room temperature for 30 min. The absorbance was examined at 517 nm in UV-VIS spectrophotometer as ascorbic acid employed as reference. If the absorbance value is low means then the free-of-charge scavenging activity will be very high.

The scavenging DPPH radical activity was calculated by utilizing the given principle-

$$\text{DPPH Scavenging Effect (\% Inhibition)} = [A_0 - A_t / A_0] \times 100$$

Where, A_0 = absorbance of the control and A_t = absorbance of tested samples at a particular time. IC_{50} = concentration of the compound required to inhibit 50% of DPPH production.

Anti-inflammatory Activity

The reaction was consisting of test extracts and 1% solution of bovine albumin fraction, pH of the reaction was used to a little amount at 37 °C HCl. The extracts were incubated at 37 °C for 20 min and then animated to 51 °C for 20 min after cooling the turbidity was deducted spectrophotometrically at 660 nm. Diclofenac sodium was used as a standard drug.

$$\text{Percentage of inhibition} = (\text{OD of Control} - \text{OD of Sample} / \text{OD of Control}) \times 100.$$

Antibacterial Studies

Bacterial filters *Viz.*, *E. coli*, *S. aureus* are engaged in these activities and Chloromphenicol is used as standard.

IR and NMR Spectral Analysis

3-(1H-indol-3-yl)-1-phenylprop-2-en-1-one (1)

From the spectrum 3-(1H-indol-3-yl)-1-phenylprop-2-en-1-one the C=O, N-H; 1599, 3440-3354 cm^{-1} ; C-N; 2361 cm^{-1} ; CH, C=C; 2921-2850, 1508 cm^{-1} ; C-O; 1168 cm^{-1} .

Molecular formula: $\text{C}_{18}\text{H}_{13}\text{NO}$: ^1H & ^{13}C NMR(300 MHz, CDCl_3): δ , 10.04 (s, 1H), 8.32 (q, $J = 9.0$ Hz, 1H), 8.142-7.956 (m, 3H), 7.83 (d, $J = 7.3$ Hz, 1H), 7.63-7.43 (m, 1H), 7.33 (q, 3H); δ 111.77, 112.07, 113.21, 116.26, 118.48, 119.97, 120.90, 121.11, 122.06, 122.56, 123.38, 124.12, 125.01, 127.82, 127.94, 128.81, 131.12, 136.03, 136.43, 136.92, 137.41, 138.79, 142.45, 189.97. MS: m/z . 247.29 $[\text{M}^+]$.

1-(4-fluorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (2)

From the spectrum 1-(4-fluorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one the C=O, N-H; 1629, 3358-3246 cm^{-1} ; CH, CH=CH; 3162, 3073 cm^{-1} ; C-F, C-O; 1221, 1041 cm^{-1} .

Molecular formula: $\text{C}_{17}\text{H}_{12}\text{FNO}$: ^1H & ^{13}C NMR (300 MHz, CDCl_3): δ , 10.04 (s, 1H), 8.35 (q, $J = 9.0$ Hz, 1H), 8.142-7.956 (m, 2H), 7.81 (d, $J = 7.1$ Hz, 1H), 7.66-7.45 (m, 4H), 7.33 (q, 3H); δ 111.74, 112.07, 113.21, 116.26, 118.48, 119.97, 120.90, 121.19, 122.06, 122.56, 123.38, 124.12, 125.01,

127.82, 127.94, 128.84, 131.12, 136.03, 136.43, 136.92, 137.41, 138.79, 142.45, 189.77. MS: m/z. 265.28 [M⁺].

3-(1H-indol-3-yl)-1-(p-tolyl)prop-2-en-1-one (3)

From the spectrum 3-(1H-indol-3-yl)-1-(p-tolyl)prop-2-en-1-one the C=O, N-H; 1646, 3387-3357 cm⁻¹; C-N, HC=CH; 2321, 3055 cm⁻¹; C-H, C=C; 3225, 1511 cm⁻¹; C-O; 1042 cm⁻¹.

Molecular formula: C₁₈H₁₅NO: ¹H & ¹³C NMR (300 MHz, CDCl₃): δ, 10.05 (s, 1H), 8.08-7.933 (m, 3H), 7.82 (d, J = 6.3 Hz, 2H), 7.60 (q, 2H), 7.46-7.26 (m, 6H), 2.42 (s, 3H); δ 25.11, 111.09, 111.32, 112.04, 112.44, 112.53, 114.77, 117.40, 119.01, 119.98, 120.06, 121.07, 121.59, 122.41, 123.19, 124.16, 129.11, 129.21, 130.41, 130.49, 136.12, 136.58, 137.29, 183.66. MS: m/z. 261.32 [M⁺].

1-(4-bromophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (4)

From the spectrum 1-(4-bromophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one the C=O, N-H; 1626, 3416-3357 cm⁻¹; C-H, C=C; 3208-3177, 1568 cm⁻¹; C=C, C-C; 3067, 2819-2782 cm⁻¹; C-O; 1121 cm⁻¹; C-Br; 670 cm⁻¹.

Molecular formula: C₁₇H₁₂BrNO: ¹H & ¹³C NMR (300 MHz, CDCl₃): δ, 10.05 (s, 1H), 8.08-7.933 (m, 3H), 7.80 (d, J = 6.3 Hz, 2H), 7.60 (q, 2H), 7.46-7.26 (m, 6H); δ 111.19, 111.32, 112.24, 112.44, 112.56, 114.77, 117.42, 119.11, 119.99, 120.06, 121.17, 121.59, 122.44, 123.19, 124.26, 129.15, 129.26, 130.47, 130.52, 136.14, 136.58, 137.33, 183.69. MS: m/z. 326.19 [M⁺].

RESULTS AND DISCUSSION

Anti – Oxidant Activity

DPPH Scavenging Assay Method

Though there are many methods available to assess the antioxidant activity of compounds, DPPH scavenging assay method is an easy and rapid method. DPPH method is also a receptive method for the antioxidant screening of synthesized organic compounds.

It is obvious beginning the data shown in Table-1 and Fig.-1. The compound **1** of the result shows the fraction of cytotoxicity for 250 mg/ml as 12.09%, 500 mg/ml as 34% and 750 mg/ml as 36% and 1000 mg/ml as 48%. The compound **2** of the result shows cytotoxicity for 250 mg/ml as 13.25%, 500 mg/ml as 26.5% and 750 mg/ml as 44.2% and 1000 mg/ml as 50.3%. The compound **3** of the result shows the % of cytotoxicity for 250 mg/ml as 12.3%, 500 mg/ml as 18.5% and 750 mg/ml as 24.3% and 1000 mg/ml as 34%. The compound **4** of the result shows cytotoxicity for 250 mg/ml as 16%, 500 mg/ml as 19.2% and 750 mg/ml as 27% and 1000 mg/ml as 43%. These inhibition values are compared with Ascorbic acid for 250 mg/ml as 23.63%, 500 mg/ml as 29.00% and 750 mg/ml as 46.25% and 1000 mg/ml as 52.05%.

Hence, this assay provided in sequence the reactivity of the samples with a constant free radical. A part of the examination on the method of the anti-oxidant activity, the capability of the compound to inhibit DPPH scavenging assay was studied. Among the **4** compounds, 1-(4-fluorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (**2**) has highest antioxidant activity.

Fig.-1

Table-1

Compounds (% of inhibition)	The concentration of the sample (µg/mL)			
	250	500	750	1000
1	12.09	34	36	48
2	13.25	26.5	44.2	50.3
3	12.3	18.5	24.3	34
4	16	19.2	27	43
Ascorbic acid (Standard)	23.63	29	46.25	52.05

Anti-inflammatory Activity

Albumen denaturation is a well-recognized cause of inflammation. Production of autoantigen in confident arthritic sickness is owing to denaturation of the protein. The method of denaturation involves a modification in electrostatic hydrogen, hydrophobic, and disulfide bonding. Aspirin was used as a standard anti-inflammation drug as shown in Table-2 and Fig.-2. The albumin denaturation technique was agreed at 100µg/ml 200µg/ml, 300µg/ml, 400µg/ml and 500 µg/ml.

Compound **1** result shows the % of cytotoxicity for 100 mg/ml as 42.2%, 200 mg/ml as 53.2%, 300 mg/ml as 56.3%, 400 mg/ml as 61.3% and 500 mg/ml as 71.3%. Compound **2** shows the % of cytotoxicity for 100 mg/ml as 36.4%, 200 mg/ml as 42.5% , 300 mg/ml as 54.7%, 400 mg/ml as 60.4% and 500 mg/ml as 66.6%. Compound **3** result shows % of cytotoxicity for 100 mg/ml as 34.3%, 200 mg/ml as 40.6% , 300 mg/ml as 52.8%, 400 mg/ml as 58.7% and 500 mg/ml as 68.9%. Compound **4** shows the % of cytotoxicity for 100 mg/ml as 43%, 200 mg/ml as 54.3% , 300 mg/ml as 58.2%, 400 mg/ml as 63.5% and 500 mg/ml as 74.2%.

These inhibition values are compared with Aspirin for 100 mg/ml as 45%, 200 mg/ml as 56.25%, 300 mg/ml as 66.20%, 400 mg/ml as 72.02% and 500 mg/ml as 82%. Albumen Denaturation show significant change when the concentrations are 100mg/ml, 200 mg/ml, 300 mg/ml, 400 mg/ml and 500 mg/ml for the compound isolated and % of cytotoxicity values are compared with Aspirin.

The in-vitro studies of Anti-inflammatory activity indicate that the inhibition percentage of the compound by Albumen Denaturation method. Inhibition percentage is higher in compound **4** compared to other compounds.

Fig.-2
Table-2

Compounds (% of inhibition)	Concentration of the sample (µg/mL)				
	100	200	300	400	500
1	42.2	53.2	56.3	61.3	71.3
2	36.4	42.5	54.7	60.4	66.6
3	34.3	40.6	52.8	58.7	68.9
4	43	54.3	58.2	63.5	74.2
Aspirin (Standard)	45	56.25	66.2	72.02	82

Anti-Bacterial Activity

The antibacterial studies of the synthesized compound using against *E. coli*, and *S. aureus* was investigated using the anti-bacterial drug of Chloromphenicol as a comparable control. From the value

in Table-3 and Fig.-3 and Fig.-4, antibacterial activity *E. coli* and *S. aureus* of synthesized compounds by disc dispersion method, antibacterial activity of synthesized compounds are possible to be well connected with its decreased dimension and figure due to enlarged surface area with improved antimicrobial activities.

Table-3

Compounds (% of Inhibition)	Organisms							
	<i>E. coli</i>				<i>S. aureus</i>			
	20	30	40	Control	20	30	40	Control
1	12	15	17	18	14	18	20	22
2	13	14	18		12	16	19	
3	9	12	16		13	16	21	
4	14	17	21		15	18	20

Fig.-3

Fig.-4

CONCLUSION

Among the 4 compounds, 1-(4-fluorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one **2** has highest anti-oxidant activity. In-vitro studies of Anti-inflammatory activity indicate that the inhibition percentage of the compound by the Albumen Denaturation method. Inhibition percentage is higher in compound **4** compared to other compounds. Antibacterial results revealed that the *E.coli*, and *S. aureus* are may be more beneficial than the aerial parts against infectious diseases. Further investigations are showing huge inhibitory action against various microorganisms.

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