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Synthesis, characterization and biological evaluation of 3-acetylindole derivatives as anti-microbial and antioxidant agents

Hitesh Kumar, Sharad Wakode and Avneet Kaur

Abstract
A series of 3-Acetylindole derivatives were synthesized by a single step process by reacting 3-acetylindole and benzaldehyde. The purity and structure confirmation of the synthesized compounds were done by TLC and 1H-NMR. The compounds were evaluated for anti-microbial and antioxidant activity. The test compound 1c, 1d, 1f, 1g, 1k and 1l showed highest anti-microbial activity and 1f, 1g, 1h and 1l show the appropriate amount of antioxidant activity.

Keywords: 3-Acetylindole, Ar Aldehyde, Anti-Inflammatory, Anti-Microbial

1. Introduction [1]

Antimicrobial agents/ Antibiotics are antibacterial substances produced by various species of micro-organism (bacteria, fungi, and action mycetes) that suppress the growth of other micro-organisms. They have been designed to inhibit or kill the infecting organism without having measurable effect on the recipient.

Antioxidants are nutrients that help to protect cells from oxidative stress which is a natural damaging physiological process. These nutrients are either present naturally in various types of food or taken as dietary supplements. They play defensive role against oxygen free radical toxicity in our body. Free radicals such as superoxide, hydroxyl and peroxide radicals are capable of damaging all types of biomolecules. They play vital role in causation and progress of oxidative stress related diseases such as Carcinogenesis, Alzheimer, Parkinson, Inflammatory diseases and Cataract. Thus, antioxidants may be considered as scavengers of free radicals. Reactive oxygen species (ROS) are formed when oxygen is present in excess and its reduction is insufficient**.** Natural occurring antioxidants are flavonoids, phenolic acid and alkaloids [2-4].

Indoles when condensed with Ar aldehydes in the presence of a base form chalcones. Chalcones are natural products and found in fruits, vegetables, spices and soya-based foodstuffs. Chalcones are the intermediates for the synthesis of biologically active heterocyclic compounds, *viz*., pyrimidine, cyclohexanone, pyrazole and isoxazole derivatives. Indoles mainly possess a various type of biological activities like anti-inflammatory [7], anti-cancer [8], anti-fungal [9], anti-viral [10] and antimalarial [11] activity etc. The 3-acetylindole derivatives have been the center of the attention of researchers over many years due to high practical value of these compounds. The 3-acetylindoles derivatives are used in the treatment of gastrointestinal, central nervous system (CNS) disorders, cardiovascular and HIV-1 integrase inhibitors [12-15].

2. Materials and Methods

2.1 Chemistry

Nuclear Magnetic Resonance (^{1}H-NMR) spectra were recorded on a Bruker using $CDCl_3$. The Chemical shift values are reported in parts per million (ppm) relative to Tetra methyl silane as internal reference. Infra-red (IR) spectra were recorded as thin films in Potassium bromide (KBr) pellets with a Bruker spectrophotometer The melting point ranges of newly synthesized compounds were determined by open glass capillary tube using Lab India's visual melting point apparatus and were uncorrected. All the commercially available reagent grade chemicals were used as received. Purity of the compound and progress of the reaction were monitored by thin layer chromatography (TLC), with detection by Ultra-violet (UV) light and/or spots were visualized by exposure to iodine vapors.

2.2 Synthesis

The title compounds were synthesized using synthetic strategy described in Scheme 1. 3-acetylindole compounds were synthesized starting from 3-acetylindole and different Ar aldehydes. The scheme of the synthesis is given in Fig.1.

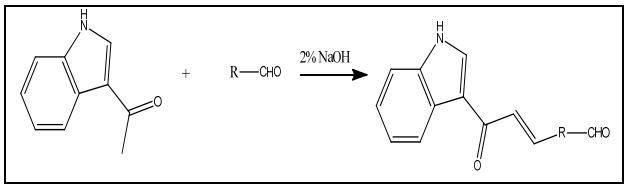

Fig 1: Scheme 1;

R= 1a = 2,4-dichlorophenyl; 1b= 4-nitrophenyl; 1c=3-bromo-4-methoxyphenyl; 1d=3-bromo-4-hydroxyphenyl; 1e=4-chloro-3-nitrophenyl; 1f=2,4,6-trimethoxyphenyl; 1g=4-hydroxyphenyl; 1h=4-flourophenyl; 1i=2-nitrophenyl; 1j=4-chlorophenyl; 1k=4-hydroxy-3-methoxyphenyl; 1l=3-ethoxy-4-hydroxyphenyl.

Scheme 1: Synthesis of 3- acetylindole dervatives

2.2.1 General procedure for synthesis of title compound (1a-l)

To a solution of 3-acetylindole (0.01 mole) in methanol (50 ml), Ar aldehyde (0.01 mole) was added in the presence of 2% sodium hydroxide. The reaction mixture was stirred for 9-10 h at room temperature. The solvent was evaporated and mixture was poured into ice water. The compound obtained was filtered, washed with water and was recrystallized from methanol.

2.2.1.1. 3-(2, 4-dichlorophenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1a)

Yield 56%, M.P.142-145 ºC; ATR-FTIR (cm-^{1}): 3300.9(NH), 2930.8(-CH str), 1628.26, 1521.25(Ar C=C), 1486.30(-CH), 1214.3 (C-N), 1164.18 (Ar-Cl), 800.91 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.84(d, 1H,-CO-CH*=CH), 7.27-7.34(m, 3H, Hd merged with H1 & H2), 7.41-7.46 (m, 4H, H8 merged with He, H3 & H6), 7.56 (s, 1H, -NH), 7.76 (d, 1H, -CO-CH=CH*)

2.2.1.2. 1-(1H-indol-3-yl)-3-(4-nitrophenyl) prop-2-en-1-one (1b)

Yield 65%, M.P. 181-183^{0}C; ATR-FTIR (cm-^{1}): 3213.60 (NH), 3142.81 (-CH str), 1603.46, 1501.22 (Ar C=C), 1485.21 (-CH), 1155.85 (C-N), 1575.01(Ar-NO_2), 750.21 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.05 (d, 1H, -CO-CH*=CH), 7.34-7.40 (m, 2H, H8 merged with H2&H1), 7.46-7.50 (s, 3H, -NH), 7.63-7.70 (m, 3H, NH merged with Ha & He), 7.77 (s, 1H, H6), 8.25 (s, 2H, Hb & Hd)

2.2.1.3. 3-(3-bromo-4-methoxyphenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1c)

Yield 88%, M.P.162-165^{0}C; ATR-FTIR (cm-^{1}): 3402.85 (NH), 3121.25(-CH str), 1641.85, 1511.59 (Ar C=C), 1501.25 (-CH), 1185.36 (C-N), 711.35 (Ar-Br), 958.02 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.82 (s, 3H, -OCH_3), 5.46 (d, 1H, -CO-CH=CH*), 6.79-6.87 (d, 1H, CO-CH*=CH merged with H8), 7.04(s, 1H, Hd), 7.31-7.40 (m, 4H, NH merged with H3, H2, He & H1), 7.58-7.61 (s, 2H, Ha & H6).

2.2.1.4. 3-(3-bromo-4-hydroxyphenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1d)

Yield 54%, M.P.192-195^{0}C; ATR-FTIR (cm-^{1}): 3385.24(NH), 3110.85(-CH str), 1611.45, 1501.89 (Ar C=C), 1485.20 (-CH), 1201.74 (C-N), 652.19 (Ar-Br), 1350.25 (Ar-OH), 958.02 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): 5.35 (s, 2H, -OH), 5.45 (s, 2H, -CO-CH=CH*), 6.80 (d, 1H, -CO-CH*=CH), 6.89 (s, 1H, H8), 6.93 (d, 1H, Hd), 7.20 (d, 1H, He**),** 7.31-7.45 (m, 3H, NH merged with Ha, H1, H2 & H3), 7.60 (s, H1 & H6).

2.2.1.5. 3-(4-chloro-3-nitrophenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1e)

Yield 64.5%, M.P.192-195^{0}C; ATR-FTIR (cm-^{1}): 3218.41 (NH), 3078.58(-CH str), 1601.47, 1514.79 (Ar C=C), 1685.74 (-CH), 1141.12 (C-N), 1159.35 (Ar-Cl), 1598.02 (Ar- NO_2), 958.02 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): 7.02 (d, 1H, -CO-CH*=CH), 7.33 (s, 2H, 1H & 2H), 7.38-7.47 (m, 2H, NH merged with H3 & H8), 7.81-7.61 (d, 2H, -CO-CH=CH*merged with He), 7.75-7.76 (s, 2H, H6 & He), 8.02 (s, 1H, Ha).

2.2.1.6. 3-(1H-indol-3-yl)-3-(2, 4, 6-trimethoxyphenyl) prop-2-en-1-one (1f)

Yield 54%, M.P.112-115^{0}C; ATR-FTIR (cm-^{1}): 3352.65 (NH), 3111.11(-CH str), 1674.87, 1509.98 (Ar C=C), 1666.44 (-CH), 1349.41 (C-N), 2850.58 (Ar-OCH_3), 974.82 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): 3.80-3.81 (s, 9H, -OCH_3*), 6.31 (s, 2H, Hb merged with Hd), 6.63 (d, 1H, -CO-CH*=CH), 7.29-7.30 (s, 2H, H1 & H2), 7.41-7.43 (d, 3H, -CO-CH=CH* merged with H3 & H8), 7.51 (s, 1H, -NH), 7.62 (s, 1H, H6).

2.2.1.7. 3-(4-hydroxyphenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1g)

Yield 52%, M.P.185-188^{0}C; ATR-FTIR (cm-^{1}): 3285.42 (NH), 3125.25(-CH str), 1641.75, 1501.59 (Ar C=C), 1674.89 (-CH), 1212.78 (C-N), 1320.25 (Ar-OH), 874.84 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): 3.78 (s, 1H, -OH), 6.85 (s, 3H, -CO-CH*=CH merged with Hb & Hd), 7.27 (s, 2H, Ha & He), 7.34-7.38 (d, 3H, H8, H2 & H1), 7.45-7.48 (m, 3H, -NH merged with –CO-CH=CH*& H3), 7.77 (s, 1H, H6).

2.2.1.8. 3-(4-flurophenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1h)

Yield 53%, M.P.192-195^{0}C; ATR-FTIR (cm-^{1}): 3385.21(NH), 3090.25(-CH str), 1684.74, 1598.39 (Ar C=C), 1699.81 (-CH), 1339.83(C-N), 1287.96 (Ar-F), 625.65 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): 5.52 (s, 1H, -CO-CH=CH*), 6.82-6.93 (d, 2H, -CO-CH*=CH merged with H8), 7.12 (s, 2H, H1 merged with Hd), 7.32-7.41 (m, 6H, -NH merged with H1, H2, H3, Ha & He), 7.61 (s, 1H, H6).

2.2.1.9. 1-(1H-indol-3-yl)-3-(2-nitrophenyl) prop-2-en-1-one (1i)

Yield 52%, M.P.189-192^{0}C; ATR-FTIR (cm-^{1}): 3485.51 (NH), 3070.45(-CH str), 1485.65, 1585.21 (Ar C=C), 1710.01(-CH), 1345.48 (C-N), 1514.20 (Ar-NO_2), 810.20 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): 6.06 (d, 1H, -CO-CH=CH*), 6.88 (s, 1H, H8), 7.06 (d, 1H, -CO-CH*=CH), 7.34 (s, 3H, H1 & H2), 7.37-7.42 (d, 1H, -NH merged with H3), 7.63-7.65 (s, 3H, He, Hd, Hc), 7.73 (s, 1H, Hd), 8.18 (s, 1H, Hb).

2.2.1.10. 3-(4-chlorop phenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1j)

Yield 52%, M.P.170-173^{0}C; ATR-FTIR (cm-^{1}): 3487.58 (NH), 3154.69(-CH stretching), 1504.20, 1475.39 (Ar C=C), 1701.20 (-CH), 1298.57 (C-N), 1165.41 (Ar-Cl), 898.98 (oop). ^{1}H NMR (300 MHz, $CDCl_3$): 5.59 (d, 1H, -CO-CH=CH*), 6.84 (d, 1H, -CO-CH*=CH), 7.00 (s, 1H, H8), 7.31-7.34 (s, 4H, H1 merged with Ha, He & H2), 7.39 (s, 2H, Hb & Hd), 7.43 (d, 2H, -NH merged with H3), 7.59 (s, 1H, H6).

2.2.1.11. 3-(4-hydroxy-3-methoxyphenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1k)

Yield 55%, M.P.163-165^{0}C; ATR-FTIR (cm-^{1}): 3499.23 (NH), 3070.20(-CH str), 1485.21, 1510.52 (Ar C=C), 1665.25(-CH), 1339.48 (C-N), 1321.20 (Ar-OH), 2840.74 (Ar-OCH_3), 765.01 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): 3.80 (s, 3H, -OCH_3), 4.08 (s, 1H, -OH), 6.80 (s, 1H, Hd), 6.85-6.87 (d, 2H, -CO-CH*=CH merged with He), 6.99 (s, 1H, Ha), 7.34 (d, 3H, H1 & H2), 7.38-7.49 (m, 3H, -NH merged with –CO-CH=CH*, H3 & H8), 7.77 (s, 1H, H6).

2.2.1.12. 3-(3-ethoxy-4-hydroxyphenyl)-1-(1H-indol-3-yl) prop-2-en-1-one (1l)

Yield 50%, M.P.175-177^{0}C; ATR-FTIR (cm-^{1}): 3102.54 (NH), 3149.84(-CH str), 1585.20, 1477.39 (Ar C=C), 1621.20 (-CH), 1274.57 (C-N), 1439.44 (Ar-OH), 741.14 (oops). ^{1}H NMR (300 MHz, $CDCl_3$): 6.80 (d, 1H, Hd), 6.85-6.87 (d, 2H, -CO-CH*=CH merged with He), 6.99 (s, 1H, Ha), 7.34 (d, 3H, H1 & H2), 7.38 (s, 3H, H8), 7.45-7.49 (m, 3H, -NH merged with H3 & -CO-CH=CH*), 7.77 (d, 1H, H6)

2.3. Pharmacological evaluation

2.3.1. Antimicrobial Activity [25, 26]

The anti-bacterial activity of the synthesized compounds was evaluated by paper disc diffusion method using nutrient agar medium against following micro-organisms: *Staphylococcus aureus, Bacillus subtilis* (Gram positive) and *Escherichia coli*, *Pseudomonas aeruginosa* (Gram negative). In the paper disc-diffusion method, paper discs impregnated with compounds dissolved in DMSO at concentration of 20, 60, and 100µg/ml were used. The microorganism culture was spread over nutrient agar media in petri-dishes and the disc impregnated with the solution was placed on the surface of the media inoculated with the bacterial strain. The plates were incubated at 35 °C for 24 hrs. After incubation, the zone of inhibition around the disc was observed. The zone of inhibition indicates that the compounds inhibited growth of micro-organism. Each testing was done in triplicate. Ciprofloxacin at concentration of 20, 60, and 100µg/ ml was used as standard drug for antibacterial activity. The results were interpreted in terms diameter (mm) of zone of inhibition represented in Table 1.

Table 1: Antibacterial activity of synthesized compounds and standard drug Ciprofloxacin determined by disc diffusion method.

Comp.	Diameter of zone of inhibition in mm											
	E. Coli			*B. Subtilis*			*S. aureus*			*P. aeruginosa*		
	20 µg/ml	60 µg/ml	100 µg/ml	20 µg/ml	60 µg/ml	100 µg/ml	20 µg/ml	60 µg/ml	100 µg/ml	20 µg/ml	60 µg/ml	100 µg/ml
1a	5.2	4.5	5.5	4.3	5.9	5.5	2.1	3.9	2.1	4.2	3.3	3.9
1b	4.2	4.9	6.8	4.1	6.6	4.4	4.3	2.78	3.1	2.9	3.4	2.8
1c	5.3	6.6	6.1	3.2	6.6	6.7	8.8	11.0	11.7	9.3	10.5	11.7
1d	10.3	9.0	8.0	7.2	5.1	6.7	3.5	4.3	5.5	4.0	6.1	3.4
1e	5.2	5.5	4.9	3.6	5.3	6.5	2.8	2.7	3.8	4.2	5.0	3.4
1f	14.0	13.5	12.5	13.1	13.0	11.8	3.3	4.3	3.5	2.8	2.9	3.1
1g	11.2	14.0	10.8	13.9	12.8	14.3	7.0	7.4	9.0	11.0	12.3	13.7
1h	14.7	13.8	12.0	11.0	11.4	12.0	11.0	9.6	10.7	11.8	12.7	9.6
1i	3.1	3.2	2.8	4.3	6.8	5.1	4.5	4.2	5.3	5.1	4.0	3.1
1j	5.3	2.8	5.1	4.3	5.1	4.3	3.9	2.1	5.1	4.4	3.1	3.9
1k	10.3	9.5	11.0	11.9	13.0	13.7	4.1	3.1	4.6	4.4	6.4	6.2
1L	11.5	13.0	14.0	14.6	11.0	8.9	4.5	5.0	4.2	6.1	6.8	2.1
Standard drug	11.0	8.5	11.0	13.0	10.5	12.6	13.2	9.0	12.8	7.6	9.7	9.8

2.3.2. Antioxidant Activity [20, 24, 25, 26]

2.3.2.1. DPPH (2-diphenyl-1-picryl-hydrazyl) Radical-Scavenging Assay

Various concentrations of synthesized compound (20µg/ml, 40µg/ml, 60µg/ml, 80µg/ml and 100µg/ml) were prepared by dissolving in DMSO. To this solution, 1ml of freshly prepared 0.1 mM methanolic solution of DPPH was added. Itwas then kept in dark for 30 min. The absorbance was measured at 517nm. DMSO was used as blank and Ascorbic acid was used as standard. The capability to scavenge the DPPH radical was calculated using the following equation and results of DPPH activity are presented in Table 2.

DPPH scavenged (%) = ($A_{control}$ - A_{test}) X 100 /$A_{control}$

Where,

$A_{control}$ was the absorbance of DPPH + methanol, and

A_{test} was the absorbance of DPPH + sample/standard

Table 2: DPPH assay results

Compounds	Percentage Inhibition (%)				
	20µg/ml	40µg/ml	60µg/ml	80µg/ml	100µg/ml
1a	47.80	30.50	40.78	54.07	67.28
1b	55.12	36.77	59.46	67.62	74.32
1c	45.80	23.11	36.77	49.42	61.60
1d	62.5	25.01	39.39	57.07	69.64
1e	60.28	29.30	47.80	59.92	74.68
1f	58.21	39.20	55.12	68.72	81.80
1g	45.80	37.40	54.98	70.80	83.97
1h	36.77	35.50	60.28	68.83	79.92
1i	80.33	40.23	58.21	71.27	85.20
1j	71.27	27.19	45.80	62.99	76.20
1k	41.20	26.00	42.75	60.15	72.67
1L	75.2	36.77	61.42	66.12	80.33
Ascorbic Acid	90.84	41.20	62.5	75.2	90.84

2.3.2.2. ABTS (2, 2'-azino-bis (3-ethylbenzthiazoline-6-sulfonicacid) radical scavenging assay

This assay is based on the ability of different compounds to scavenge 2, 2-azino-bis (ethylbenzthizoline-6-sulfonic acid) radical cation. ABTS radicals have characteristic absorbance at 734nm. This absorbance decreases when radical is reduced by any antiradical compound. The decrease in the absorbance can be measured using UV-VIS spectrophotometer at 734nm

For ABTS assay, the stock solutions of 7mM ABTS and 2.4mM potassium persulfate was prepared. The working solution was then prepared by mixing the two stock solutions in equal quantities (1:1) and allowing them to react for 12h at room temperature in the dark. The solution (1ml) was then diluted with 60 ml methanol to obtain an absorbance of 0.706±0.001 units at734nm using the UV spectrophotometer. Methanolic solutions of all compounds as well as ascorbic acid were prepared in the concentration of20ug/ml, 40ug/ml, 60ug/ml, 80ug/ml and 100ug/ml. Compounds/Ascorbic acid (1ml) of different concentration was allowed to react with 1ml of the $ABTS^+$ solution and the absorbance was taken at 734nm using UV spectrophotometer. The $ABTS^+$ scavenging capacity of the extract was compared with that of Ascorbic acid and percentage inhibition calculated using the following equation and results of ABTS activity are presented in Table 3.

ABTS radical scavenging activity (%) = $Abs_{control} - Abs_{sample}/Abs_{control} \times 100$

Where,

$Abs_{control}$ was the absorbance of ABTS radical + methanol, and

Abs_{sample} was the absorbance of ABTS radical + sample/standard.

Table 3: ABTS Assay results

Compounds	Percentage Inhibition (%)				
	20µg/ml	40µg/ml	60µg/ml	80µg/ml	100µg/ml
1a	36.6	28.6	38.9	45.7	59.3
1b	53.9	38.7	50.4	57.1	66.6
1c	35.1	26.7	35.9	47.7	55.9
1d	30.9	30.1	36.6	54.3	65.4
1e	43.2	32.9	42.8	56.9	68.7
1f	37.9	40.1	51.9	58.3	71.6
1g	46.7	38.5	50.8	58.9	71.9
1h	26.7	37.9	52.6	59.6	70.1
1i	40.1	43.2	53.9	61.9	72.5
1j	43.2	29.9	40.6	57.5	70.3
1k	30.9	30.9	38.8	57.2	64.9
1L	34.9	35.1	48.9	61.2	70.9
Ascorbic Acid	28.6	46.7	57.3	67.6	79.8

3. Results & Discussion

The compounds were synthesized in moderate to good yield. Purity of compounds was determined by TLC on silica gel G plates. The spots were detected by exposure to iodine vapors. Synthesized compounds were characterized by spectral analysis (Fourier Transform Infra-red and ^{1}HNMR). The spectra were found to be in agreement with the assigned molecular structures. Among the synthesized compounds 1d, 1f and 1h showed higher activity against *B.subtilis* when compared to standard, while, 1k and 1l also showed higher activity against *E. coli.* Similarly, compounds 1c, 1g, and 1h showed appreciable activity against *S.aureus* and *P. aeruginosa*. For antioxidant activity, compounds 1f, 1g, 1h and 1l showed maximum antioxidant activity compared to Ascorbic acid.

4. Conclusion

A series of 3-acetylindole derivatives were synthesized. All the synthesized compounds showed some anti-microbial and antioxidant activity. Among the synthesized compounds 1d, 1f and 1hshowed higher activity against *B. subtilis* when compared to standard, while, 1k and 1l also showed higher activity against *E. coli.* Similarly, compounds 1c, 1g, and 1h showed appreciable activity against *S.aureus* and *P. aeruginosa*. For antioxidant activity, compounds 1f, 1g, 1h and 1l showed maximum antioxidant activity compared to Ascorbic acid.

5. References

1. Achar KC, Hosamani KM, Seetharamareddy HR. *In-vivo* analgesic and anti-inflammatory activities of newly synthesized benzimidazole derivatives. Eur. J. Med. Chem. 2010; 45:2048-2054.
2. Tripathi KD. Essentials of Medical Pharmacology, Edn 6, Jaypee Brothers Medical Publishers (P) Ltd., New Delhi. 2007, 184-187.
3. Sharma HL, Sharma KK. Principles of Pharmacology, Paras Medical Publisher, New Delhi. 2007, 367-368.
4. Finkel R, Clark MA, Cubeddu LX, Harvey RA, Champe PC. Lippincott's Illustrated Review: Pharmacology, Edn 4, Lippincott Williams & Wilkins, New Delhi. 2009, 499-502.
5. Borne R, Levi M, Norman W. Nonsteroidal Anti-inflammatory drugs. In: Lemke LT, Williams DA, Roche VF, Zito SW, Editors. Foye's Principles of Medicinal Chemistry, Edn 6, Lippincott Williams & Wilkins, New Delhi. 2008, 954-980.
6. Wilson LM. In: Price SA, Wilson LM, Editors. Pathophysiology: Clinical Concepts of Disease Processes, Mosby, St. Louis, Missouri. 2003, 44-61.
7. Radwan MAA, Ragab EA, Nermien M. Synthesis and biological evaluation of new 3-substituted indole derivatives as potential anti-inflammatory and analgesic agents. Bioorg. Med. Chem. 2007; 15:3832-41.
8. Singh P, Mittal A, Bhardwaj A, Kaur S. 1- Toluene-sulfonyl-3-[(30-hydroxy-50-substituted)-c butyrolactone]- indoles:Synthesis,COX-2 inhibition and anticancer activities. Bioorg. Med. Chem. Lett. 2008; 18:85-89.
9. Ryu CK, Lee JY, Park R, Ma M. Synthesis and antifungal activity of 1H-indole-4,7-diones. Bioorg. Med. Chem. Lett. 2007; 17:127-31.
10. Perumal T, Lakshmi NV, Thirumurugan P, Noorulla KM. InCl3 mediated one-pot multi component synthesis, antimicrobial, antioxidant and anticancer evaluation of 3-pyranyl indole derivatives. Bioorg. Med. Chem. Lett. 2010; 20:5054-61.
11. Mazzei M, Giampieri M, Balbi A, Colla PL, Ibba C. Antiviral activity of indole derivatives. Antiviral Research. 2009; 83:179-85.
12. Liu K, Sun J, Lou H, Dai S, Xu H. Indole alkaloids from Nauclea officinal is with weak antimalarialActivity. Phytochemistry. 2008; 69:1405-10.
13. Abdel-Rahman AAH, Abdel-Megied AES, Hawata MAM, Kasem ER, Shaaban MT. Synthesis and antimicrobial evaluation of some chalcones and their

derived pyrazoles, pyrazolines,isoxazolines, and 5,6-dihydropyrimidine-2- (1H)-thiones. Monatsh. Chem. 2007; 138:889-897.
14. George S, Waran MP, Chakraborty A, Ravi TK. Synthesis and evaluation of the biologicalactivities of some 3-[5-(6-methyl-4-aryl-2-oxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1,3,4-oxadiazol--2-yl]-imino-1,3-di-hydro-2*H*-indol- 2-one derivatives. Acta. Pharm. 2008; 58:119-129.
15. Metawally MA, Shaaban S, Abdel-Wahab BF, Gamal A. 3-acetylindole:synthesis,reactions and Biological activity. Current Organic Chemistry. 2009; 13:1475-1495.
16. Winter CA, Risley EA, Nuss GW. Anti-inflammatory and related properties of 4-(pbiphenylyl)-3-hydroxybutyric acid. Proc. Soc. Exp. Biol. Med. 1962; 111:544–547.
17. Akhtar S. Benzimidazole derivatives. International journal of scientific and engineering research. 2013; 4:1674.
18. Satyanarayana U, Chakrapani U. Biochemistry. New Delhi: Elsevier Health Sciences APAC. 2013; 6:1201.
19. Marinova G. Evaluation of the methods for determination of the free radical scavenging activity by DPPH. Bulgarian journal of Agricultural Sciences. 2011; 17(1):11-24.
20. Roberta Re, Nicoletta Pellegrini, Anna Proteggente, Ananth Pannala, Min Yang, Catherine Rice-Evans. Antioxidant Activity Applying An Improved ABTS Radical Cation Decolorization Assay; Free Radical Biology & Medicine. 1999; 26(9/10):1231-1237.
21. Bhuyan PJ, Deb ML. Uncatalyzed Michael addition of indoles: synthesis of some novel 3-alkylated indoles via a three component reaction in solvent free conditions. Tetrahydron Letters. 2007; 48:2159-63.
22. Tawfeq M, Alsadoun J. Synthesis of indole derivatives, jawahar lal Nehru technological university, college of engineering, kukatpally, Hyderabad. 2010; 6:25-28.
23. Srivastva SK, Verma S, Srivastva SD. 'Syntheis, characterization and biological activity of 1, 3-thiazolidin-4-one derivatives of 2-mercapto-5-methyl-1,3,4-thiadiazole, J. Chem. Pharm. Res. 2010; 2:270-276.
24. Perumal T, Lakshmi NV, Thirumurgan P, Noorulla KM. InCL3 mediated onepot multicomponent synthesis, antimicrobial, antioxidant and anticancer evaluation of 3-pyranyl indole derivatives. Bioorg. Med. Chem. Lett. 2010; 36:915-923.
25. Metawally MA, Shaaban S, Abdel-Wahab BF, Gamal A. 3-acetylindole: synthesis, reaction and biological activity, Current Organic Chemistry. 2009; 2:845-850.
26. Harold C, Neu, Thomas D. Gootz, Antimicrobial Chemotherapy Medical Microbiology.4th Ed., University of Texas. 1996; 3:102-105.