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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL INDOLE DERIVATIVES

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ABSTRACT:

Indole derivatives have been a topic of substantial research interest and continue to be one of the most active areas of heterocyclic chemistry, because of their natural occurrence and pharmacological activities. We reported here in the synthesis of **3(1H-indol-3-yl)-1-[4-(arylidene) phenyl] prop-2-en-1-one** and **2-amino N- arylidene-4-(1H-indol-3-yl)-6-phenylpyrimidin.** The required indole-3-aldehyde has been prepared by Vilsmeir Haack reaction. Antimicrobial activity is determined based on their Invitro activity in purecultures. Invitro susceptibility testing done by Turbidimetric method & Agar diffusion method. The antimicrobial screening results presented on above table reveals that compounds **B-4, B-5** exhibited good activity against *S.aureus* and *E.Coli*, at 50 µg/ml, but at 100 µg/ml and other have shown moderate activity against *S.aureus, E.Coli*. The compounds **A-2, A-3** exhibited Good activity against S.aureus and E.coli, at 50 µg/ml, but at 100 µg/ml and other have shown moderate activity against *S.aureus, E.Coli*.

KEYWORDS: Ciprofloxacin, Fluconazole, IR spectra, 1HNMR, TLC, Antifungal activity, Antibacterial activity, Staphylococcus aureus, E.Coli, Candila albicans.

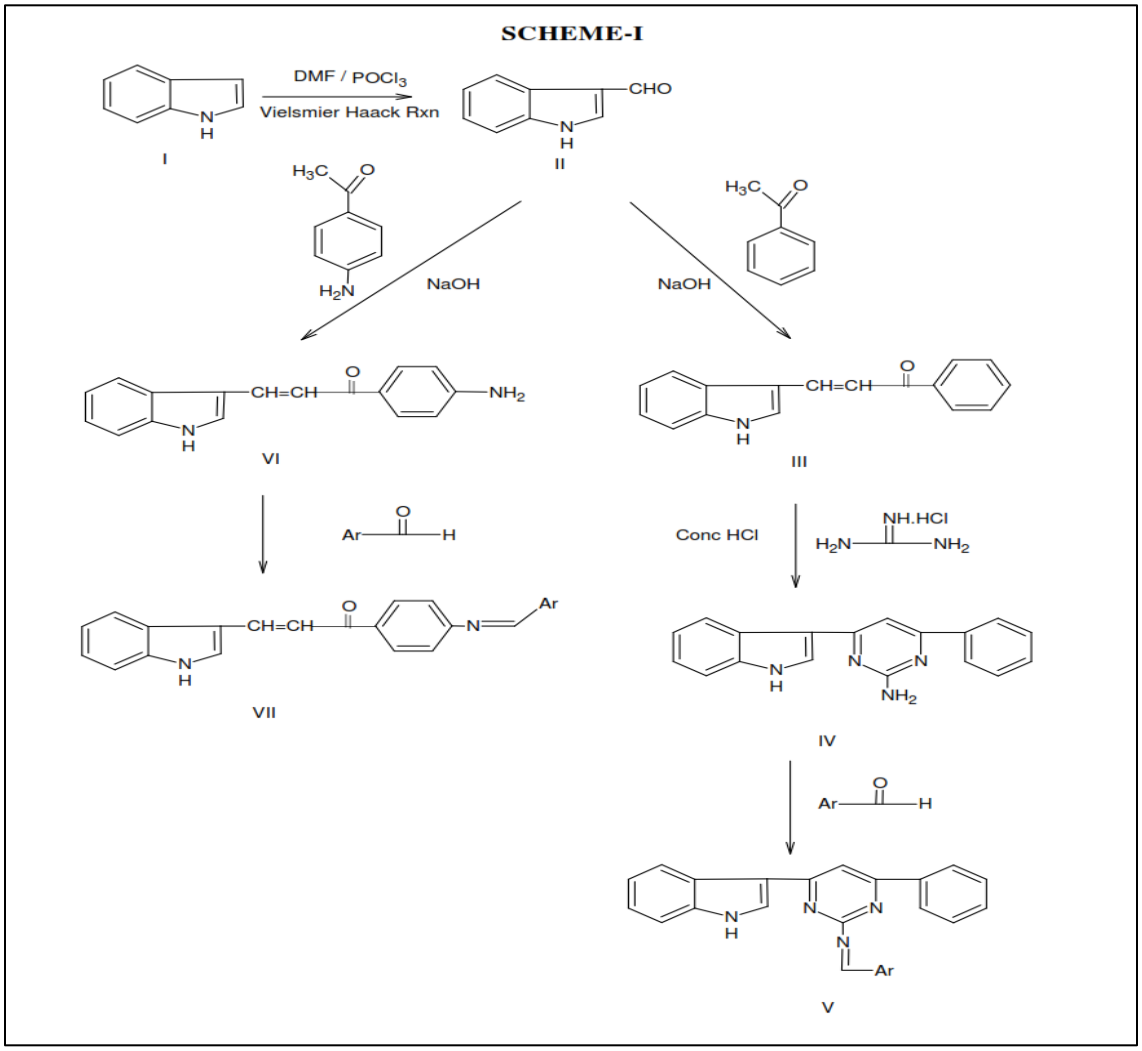
INTRODUCTION

It is a rational approach towards the drug design and development, based upon the various physical and physiochemical parameters[1]. That's why most of the drugs in practice are derivatives of known molecules, whether it is β-lactam antibiotics (Penicillin G, Penicillin V, and Ampicillin), Irreversible proton pump inhibitors (Omeprazole, Lansoprazole, Rabeprazole), or CNS drugs such as BDZ derivatives (Diazepam, Clonazepam etc).The earlier sources of drugs were from plants, animals and mineral sources, but due to the lack of potential action and definitive cure and sometime more toxicity, the discovery of new drugs that are more potential and less toxic is essential[1-4]. The chemistry of indole nucleus has gained importance, as many of them exhibit pronounced bio active nature amongst different heterocyclic systems. Many naturally occurring pigments, vitamins, and antibiotics are heterocyclic compounds, as are most hallucinogens. Modern society is dependent on synthetic heterocyclic for use as drugs, pesticides, dyes, and plastics. The most common heterocyclic are those having five- or six-membered rings and containing heteroatoms of nitrogen (N), oxygen (O), or sulfur (S). The best known of the simple heterocyclic compounds are pyridine, pyrrole, furan, and thiophene[5,6]. A molecule of pyridine contains a ring of six atoms—five carbon atoms and one nitrogen atom. Pyrrole, furan, and thiophene molecules each contain five-membered rings, composed of four atoms of carbon and one atom of nitrogen, oxygen, or sulfur, respectively. Pyridine and pyrrole are both nitrogen heterocyclic their molecules contain nitrogen atoms along with carbon atoms in the rings. The molecules of many biological materials consist in part of pyridine and pyrrole rings, and such materials yield small amounts of pyridine and pyrrole upon strong heating. In fact, both of these substances were discovered in the 1850s in an oily mixture formed by strong heating of bones. Today, pyridine and pyrrole are prepared by synthetic reactions. Their chief commercial interest lies in their conversion to other substances, chiefly dyestuffs and drugs. Pyridine is used also as a solvent, a waterproofing agent, a rubber additive, an alcohol denaturant, and a dyeing adjunct. Furan is an oxygen-containing heterocyclic employed primarily for conversion to other substances (including pyrrole). Furfural, a close chemical relative of furan, is obtained from oat hulls and corncobs and is used in the production of intermediates for nylon. Thiophene, a sulfur heterocyclic, resembles benzene in its chemical and physical properties. It is a frequent contaminant of the benzene obtained from natural sources and was first discovered during the purification of benzene. Like the other compounds, it is used primarily for conversion to other substances. Furan and thiophene were both discovered in the latter part of the 19th century. In general, the physical and chemical properties of heterocyclic compounds are best understood by comparing them with ordinary organic compounds that do not contain hetero-atoms[7-9].

Indole and its derivatives have occupied an in imitable place in the chemistry of nitrogen heterocyclic compounds. From simple derivatives to complex alkaloids, Indole is found in an immensely varied range of biologically significant natural products and showed numerous biological activities.

METHODOLOGY[10,11]:

A literature survey reveals that very few references are available on the synthesis of pyrimidine associated with indole compounds and its Schiff bases. We reported here in the synthesis of **3(1H-indol-3-yl)-1-[4-(arylidene) phenyl] prop-2-en-1-one** and **2-amino N- arylidene-4-(1H-indol-3-yl)-6-phenylpyrimidin.** For this purpose, the required indole-3-carbaldehyde has been synthesized and made use of as specified in **SCHEME-I.** The required indole-3-aldehyde has been prepared by Vilsmeir Haack reaction from indole (**II)** was reacted with 4-aminoacetophenone and acetophenone in ethanolic NaOH to obtain **3-(1H- indol-3-yl)-1-phenylprop-2-en-1-one** (**III)** and **1-(4-aminophenyl)-3-(1H-indol-3-yl) prop-2-en- 1-one (VI)**by adopting the standard procedure. These were identified by the literature melting point and IR data. Similarly**2-amino-(1H-indol-3yl)-6-phenylpyrimidine** (**III)** was prepared by the condensation of guanidine hydrochloride with hydrochloric acid in absolute ethanol. Adopting a standard procedure. This was identified by the literature melting point and IR spectral data. **Synthesis of 2-N-arylidene-4-(1H-indol-3-yl)-6-phenylpyrimidine (V):** Since the compound (**IV)** possess free amino group at 2-position of pyrimidine ring. This free amino group can be exploited for further synthetic manipulation to undergo its characteristic nucleophilic addition followed by elimination of water molecule with different aromatic aldehyde to yield Schiff base. According this method compound (**IV)** reaction with aromatic aldehyde in the presence of absolute ethanol and catalytic amount of glacial acetic acid afforded **2-N-arylidine-4-(1H-indol-3-yl)-6 phenylpyrimidines (V_{1-05}).** Then this has been purified by recrystallization from ethanol and subjected to analytical and spectral analysis. The compound obtained from all such reaction have been characterized as according **2-N-arylidene-4-(1H-indol-3-yl)-6- phenylpyrimidines (V_{1-05}).** For example: 2**-amino-4-(1H-indol-3-yl)-6-phenylpyrimidine (VI)** with 4-nitrobenzaldehyde in equimolar ratio under identical experimental condition has been resulting in the formation of product. It has been purified by recrystallization from ethanol to obtain pure recrystallized solid M.P-123^{0}C.



The IR spectrum of compound: (In KBr fig. 2) has exhibited characteristic observation frequencies (in cm^{-1}) at 3105(NH), 3056(Ar-H), 1602(C=N).**^{1}HNMR spectrum of compound: (In DMSO-d_6 fig. 3)** has showed the characteristic proton signals (in σ, ppm) at 10.160 (s, 1H, NH), 7.034-8.361 (m, 13H, Ar-H 1H pyrimidine proton and 1H of indole proton) and 6.984 (s, 1H, -N=CH) Similarly treatment of compound **(IV)** has different aromatic aldehyde and the single product uniquely obtained in each reaction could be characterized as their respective **2-N- arylidene-4-(1H-indol-3-yl)-6-phenyl pyrimidine (V).**Thus five of them have been prepared and their characterization data are presented in the **Table no. 1.** The **1-(4-aminophenyl)-3-(1H-indol-3-yl) prop-2-en-1-one** (**VI)** has been subjected to addition with different aromatic aldehydes in reflux with ethanol under the influence of glacial acetic acid have **(VII$_{1-05}$)** in good yield. This has been purified by ethanol and subjected for analytical and spectral analysis. The compound obtained from all such reaction have been characterization as corresponding **3-(1H-indol-3yl)-1-[4-(arylidene) phenyl] prop-2-en-1-one.** To present such reaction in detail as a model the

reaction between **1-(4-aminophenyl)-3-(1H-indol- 3-yl) prop-2-en-1-one (VI)** the **p-methyl benzaldehyde** has been chosen.[12,13]

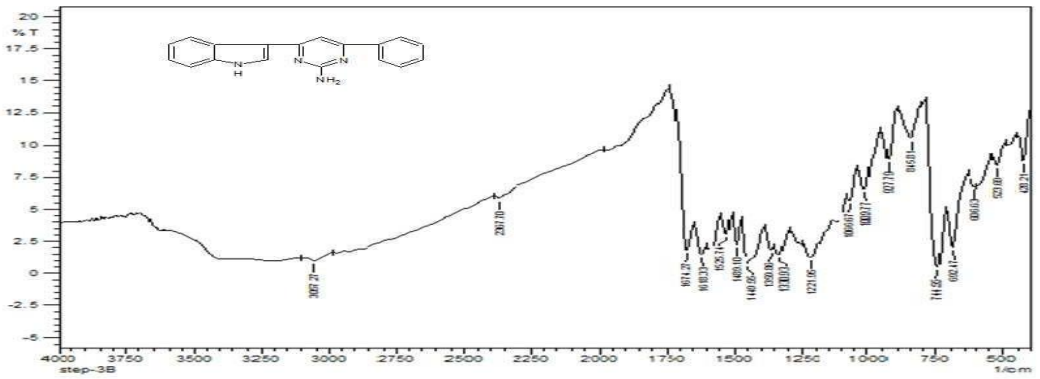


Fig. 1- IR Spectra of 4-(1H-indol-3-yl)-6-phenylpyrimidin-2-amine (compound IV)

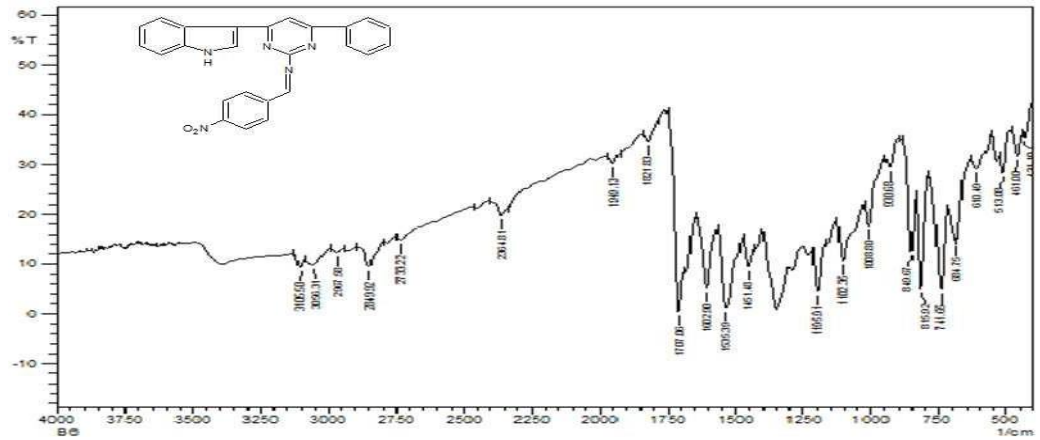


Fig-2: IR Spectraof4-(1H-indol-3-yl)-N-[(1Z)-4-nitrocyclohexa-2, 4-dien-1-ylidene]-6-phenyl pyrimidin- 2-amine

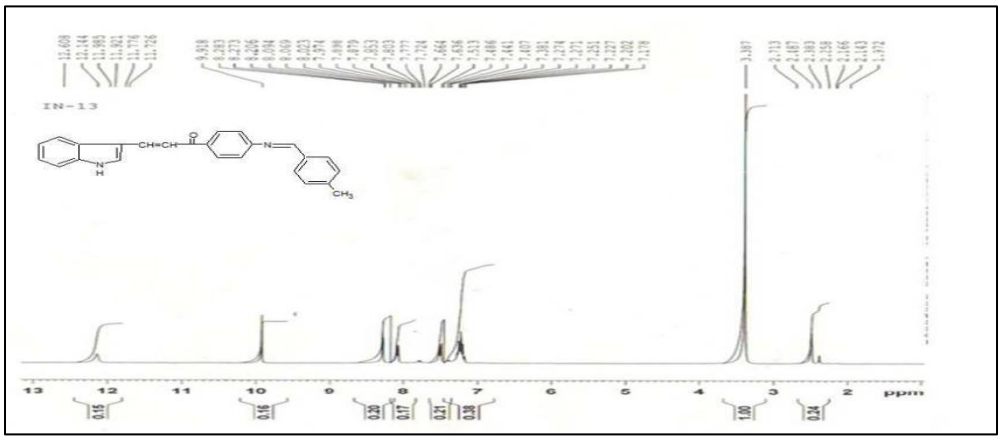


Fig: 3 1HNMR spectra of 4-(1H-indol-3-yl)-N-[(1Z)-4-nitrocyclohexa-2, 4-dien-1-ylidene]-6-phenylpyrimidin-2-amine

Action of 1-(4-aminophenyl)-3-(1H-indol-3-yl) prop-2-en-1-one with aromatic aldehydes (VI):

The reaction in equimolar ratio has been heated under reflux in ethanol under the influence of glacial acetic acid for 14 +hrs. After cooling the reaction mixture was poured into ice cold water then a solid product obtained was filtered and washed with water. It has been purified by recrystallization from ethanol to obtain dark crystalline compound m.p.215-220^{0}C. **IR Spectrum of the compound: (In KBr fig.5)** it has been found to exhibit characteristic absorption frequencies (in cm^{-1}) at 3250 (-NH_2), 3043 (-NH), 2979 (Ar-H), 1615 (C=N). **1HNMR Spectrum of the compound: (in DMSO-d_6 fig. 6)** it has showed its characteristic proton signals in (inσ, ppm) at 2.487 (s, 3H,-Ar-CH_3), 8.023 (d,1H, -CH=CH), 8.206 (s, 1H, - N=CH), 7.202-7.174 (m,12H, Ar-H), 9.918 (s,1H,=CH-C=O) and 12.144 (s,1H, -NH).Similarly **1-(4-aminophenyl)-3-(1H-indol-3-yl) prop-2-en-1-one** subjected to addition with the rest of the ten aldehyde. The product obtained in each such reaction has been characterized as corresponding**3-(1H-indol-3-yl)-1-[4-(arylidene) phenyl] prop-2-en-1-one. (VII)** Physical analytical and spectral data of the synthesized compound a represented in the **Table no 2.**

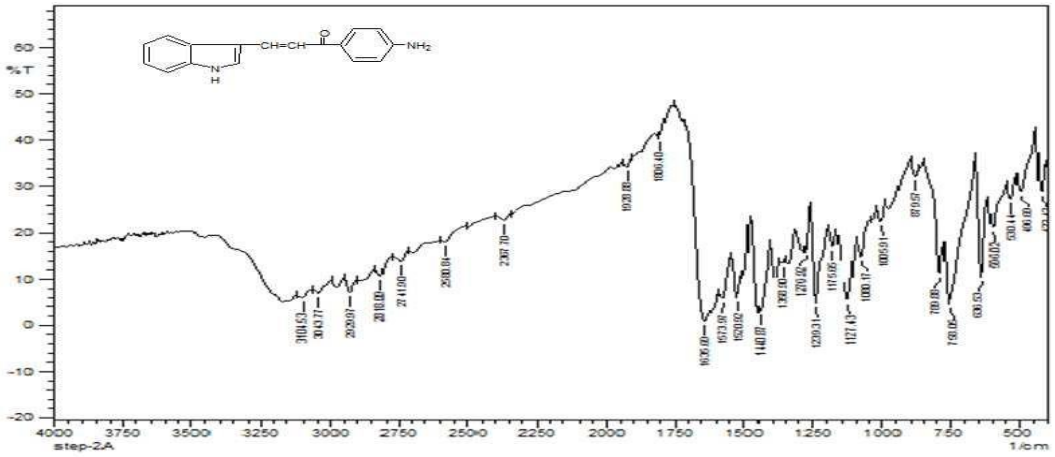


Fig-4: IR Spectra of 1-(4-aminophenyl)-3-(1H-indol-3-yl) prop-2-en-1-one

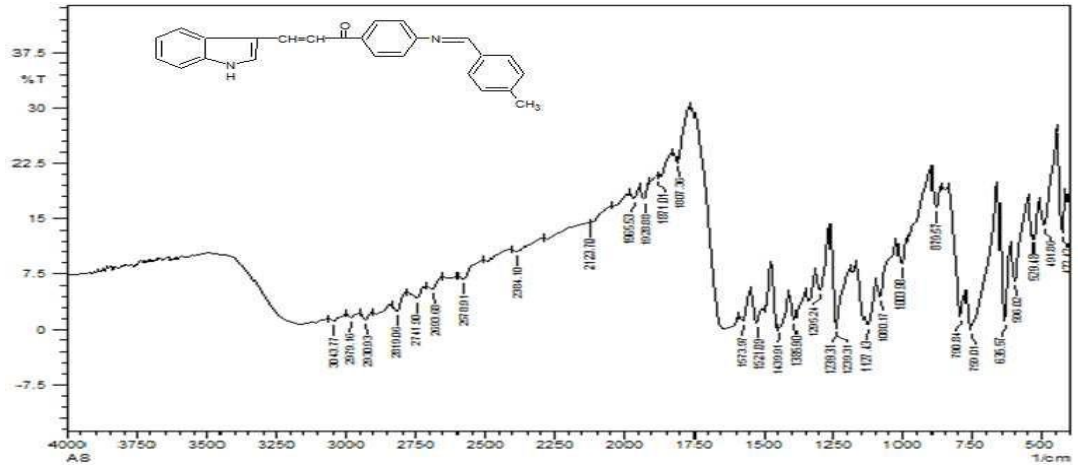


Fig.-5: IR Spectra of 3-(1H-indol-3-yl)-1-(4-{[(4-methylphenyl)methylene]amino} phenyl) prop-2-en-1-one

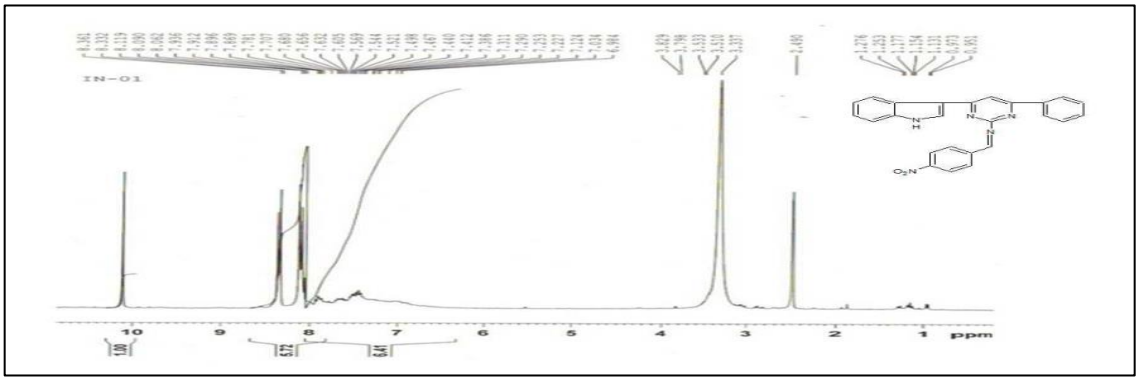


Fig -6: 1HNMR Spectra of 3-(1H-indol-3-yl)-1-(4-{[(4- methyl phenyl) methylene] amino} phenyl) prop-2-en-1-one

Table 6.1: Physical data of the synthesized compound (V_{B1-05}):

S.N.	Compound Code	Ar	Melting point	Yield %	Molecular formula	Molecular weight
1	B1	C_6H_5	118-125°C	69.52	$C_{25}H_{18}N_4$	374
2	B2	3-OCH_3-C_6H_4	130-135°C	76.14	$C_{26}H_{20}N_4O$	404
3	B3	4-OCH_3-C_6H_4	125-130°C	62.82	$C_{26}H_{20}N_4O$	392
4	B4	3,4,5(CH3)3- C6H2	112-117°C	46.30	C28H24N4	416
5	B5	4-CH3-C6H4	130-145°C	69.76	C26H20N4	352

Table 2: Physical data of the synthesized compound (VII_{A1-05}):

S.N.	Compound Code	Ar	Melting point	Yield %	Molecular Formula	Molecular Weight
1	A1	C_6H_5	250-252°C	48.27	$C_{24}H_{18}NO$	350
2	A2	4-Br-C_6H_4	220-240°C	56.33	$C_{24}H_{17}NOBr$	429
3	A3	C_8H_7	175-190°C	51.01	$C_{26}H_{20}N_5O_2$	364
4	A4	3-OCH_3-C_6H_4	201-230°C	43.38	$C_{25}H_{20}NO$	381
5	A5	4-N-$(CH_3)_2$-C_6H_4	190-214°C	50.01	$C_{26}H_{23}N_2O$	379

SPECTRAL STUDIES[12,13,14]:

IR Spectra: The peaks in IR Spectrum give an idea about the probable structure of the compound IR region ranges between 4000-666 cm^{-1}. Quanta of radiation from this region of the spectrum correspond to energy differences between different vibrational levels of molecules. The compounds were recorded on SHIMADZU FTIR-8400S spectrophotometer shows different vibration levels of molecules. Spectrophotometer by using Nujols technique.

1HNMR Spectra: NMR spectroscopy enables us to record differences in magnetic properties of the various magnetic nuclei present, and to deduce in the large measure about the position of these nuclei are within the molecule. We can deduce how many different kinds of environment are there in the molecules and also which atoms are present in neighboring groups. The proton NMR spectra enable us to know different chemical and magnetic environments corresponding to protons in molecules. The samples are analyzed on advance 300 MHz spectrometer.

Table 3: IR and ^{1}HNMR spectral data of the synthesized compound (V_{B1-05}):

S.N.	Comp. Code	I.R. Spectral Data (cm^{-1})					1HNMR (in σ ppm)
		Ar	Ar –H	CHO	NH	C=N	---
1	B1	C_6H_5	3057	1668	3372	2240	---
2	B2	3-OCH_3-C_6H_4	3057	1696	3360	2260	---
3	B3	4-OCH_3-C_6H_4	3044	1645	3322	2234	NMR-10.160(s,1H, -NH), 7.034-8.361(m,13H,Ar-H), 6.984(s,1H,-N=CH)
4	B4	4,5$(CH_3)_3$- C_6H_2	3040	1605	3344	2238	---
5	B5	4-CH_3-C_6H_4	3056	1698	3358	2235	---

Table 4: IR, and 1HNMR spectral data of the synthesized compound (VII_{A1-05}):

S.N.	Comp. Code	I.R. Spectral Data (cm^{-1})					1HNMR (in σ ppm)
		Ar	Ar –H	C=O	NH	C=N	----
1	A1	C_6H_5	3043	1663	3344	2240	----
2	A2	4-Br-C_6H_4	3171	1740	3332	2255	----
3	A3	C_8H_7	3157	1758	3350	2240	----
4	A4	3-OCH_3-C_6H_4	3104	1684	3325	2285	NMR- 2.487 (s, 3H,-Ar-CH_3), 8.023 (d, 1H,- –CH=CH-), 8.206 (s,1H, -N=CH) 7.202-7.174 (m,12H,Ar-H), 9.918 (s,1H, =C-C=O),12.144 (s, 1H, -NH)
5	A5	4-N-$(CH_3)_2$-C_6H_4	3158	1663	3389	2267	----

BIOLOGICAL EVALUATION[15]:

Pharmacological evaluation involves testing the microbial susceptibility to chemotherapeutic agents. Determination of antimicrobial effectiveness against specific pathogens is essential to proper therapy. Testing can show which agents are more effective against a pathogen and give an estimate of proper therapeutic dose. Some ideas of the effectiveness of amino therapeutic agent a pathogen can be obtained from the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of a drug that prevents growth of particular pathogen the minimal lethal concentration (MLC) is the lowest concentration that kills pathogens. Antimicrobial activity is determined based on their Invitro activity in purecultures. Invitro susceptibility testing done by the following methods. The following two are the methods available for screening the antimicrobial substances:

Turbidimetric method: By this method the minimum concentration of the antimicrobial substances required to inhibit the growth of microbial culture in a uniform bacteriological fluid medium, containing the specified antimicrobial substances, which otherwise is favorable for the rapid growth is determined. The minimum concentration required for inhibiting the growth is called minimum inhibitory concentration (MIC). A graded concentration of the antimicrobial substances in sterile fluid nutrient media is prepared. All of them are inoculated with a loop of specific microorganism. A positive control, a negative control and a blank is also determined. They are incubated at 37 ^{o}C for 24 hours or necessary conditions depending on the organism chosen. Among the different concentration of the substance, the least one, which inhibit the growth of the microorganism, is noted visually or by measuring the percentage transmittance or absorbance at 530 nm against a blank.

Agar diffusion method: This method gives the extent of growth of the microorganism, inoculated in to a solid nutrient agar bed by the antimicrobial substances. The test substances is kept in a cup made of agar bed, diffuses in to it and inhibit the growth of the microorganism. The diameter of the zone of inhibition is measured in comparison with suitable drug substances, is considered as potency of the substances. The diameter of zone inhibition is directly proportional to the concentration of the drug substances added in to the cup, thickness of the agar bed, and diffusion coefficient of the antimicrobial substances in to the agar cup, sensitivity of the microorganism to the test substances and the temperature. The appropriate media is sterilized and cooled to 42^{o}C, incubated with the test organism, mixed uniformly and poured in to the petri dishes and cooled. Bores are made into it, specified test solution is added and left at room temperature for 30 minutes. Incubate at 37^{o} C for 24 hours. The zone of inhibition is measured in cm/mm.

Methods of obtaining pure cultures: The streak plate method of obtaining pure culture involves spreading bacteria across a sterile, solid surface such as agar plate so that the progeny of a single cell can be picked up from the surface and transfer to a sterile medium. The pour plate method of obtaining pure culture involves serial dilutions, transferring to melted agar, a specific volume of the dilution containing a few organisms and picking up cells from colony of agar.

Culture media:

- In nature, microbes grow on natural media or the nutrients available in water, soil and living or dead organic matters.
- In laboratory, microbes grow in artificial media.
- Synthetic media- Consists of known quantities of nutrients.
- Complex media- Consists of nutrients of reasonably well-known composition that vary in composition from batch to batch. Most routine laboratory culture makes use of peptones (general purpose media) or digested meat or fish proteins. Other cultures used are yeast extracts, casein, serum, whole blood or heated whole blood (Enriched media). Diagnostic media.

Types of media:

- **Selected media:** They encourage growth of some organism and inhibit the others.
- **Differential media:** They allow the growth of different kinds of colonies to grow on the same plate to be distinguished from one another.
- **Enriched media:** They provide a nutrient that fastens the growth of organisms.

Methods:

1. Method followed: agar diffusion method.
2. Requirements: Petri dishes, glass syringes, cork borers, inoculation loop, cotton

Working procedure: Antimicrobial assay- Cup plate method

Sample preparation- (Compounds)Stock solutions of the synthesized compounds and standard drug used were prepared in dimethyl formamid taken in the concentration of 0.1 mg/ml and 1 mg/ml. volume- 50 µl, 100 µl.

Standard drugs-

- Ciprofloxacin as antibacterial agent
- Fluconazole as antifungal agent.

Microorganism used-

- Staphylococcus aureus, Protens Mirabilis (G+ve)
- E. coli, Klessiella pneumonia (G-ve) Aspergilusniger,
- Candida albicans (Fungi)

Composition of media:

Nutrient agar media (For bacteria)

Beef extract	4 gms
Peptone	5gms
Agar	20 gms
Sodium chloride-	5 gms
Distilled water-	1000 ml
Ph	6.8-7.2

Potato dextrose media (For fungi)

Potato dextrose agar	39gms
Distilled water	1000ml

Procedure: The Petri dishes were washed thoroughly and sterilized in hot air oven at 160^{o} C for one hour. 30 ml of sterile nutrient agar media for bacteria and potato dextrose agar media for fungi was poured in to sterile Petri dishes and allowed to solidify. The plates were incubated at 37^{o}C for 24 hours to check for sterility. The medium was seeded with the organism by spread plate method using sterile cotton swabs. Bores were made on the medium using sterile borer and 2 mg/ml of Ciprofloxacin for bacteria and 2 mg/ml Fluconazole for fungi were taken as standard reference while the sample preparation were made 0.1 mg/ml and 1 mg/ml in DMSO. The Petri dishes were kept in refrigerator at 4^{o} C for 15 minutes, allowing diffusion to take place. The Petri plates were incubated at 37^{o} C for 24 hours and zone of inhibition were observed and measured using a scale. Antimicrobial activities of all the compounds were carried out against all microorganisms and fungi organism. [29,30,31]

Table no.5 Anti-bacterial activity data of synthesized compound (B1-B5):

S.N.	Compound	Concentration µg/ml	E.coli	S.Aureus
1	B-1	50	9	10
		100	12	14
2	B-2	50	8	11
		100	14	14
3	B-3	50	7	13
		100	12	13
4	B-4	50	12	14
		100	15	13
5	B-5	50	14	13
		100	13	14
6	Ciprofloxacin	50	24	26

Zone of inhibition of synthesized compounds:

Note: 6-9 mm poor activity, 10-12 mm moderate activity, 13-15 above good

Table no. 6 -Anti-bacterial activity data of synthesized compound (A1-A5):

Sr. No	Compound	Concentration (µg/ml)	E.coli	S.Aureus
1	A-1	50	9	10
		100	8	9
2	A-2	50	12	11
		100	11	10
3	A-3	50	12	11
		100	10	11
4	A-4	50	6	7
		100	9	10
5	A-5	50	8	11
		100	11	9
6	Ciprofloxacin	50	28	24

Zone of inhibition of synthesized compounds:

Note: 6-9 mm poor activity, 10-12 mm moderate activity, 13-15 above good

Table no: 7-Anti-fungal activity data of synthesized Compound (B1-B5):

S.N.	Compound	Concentration (µg/ml)	Candida albicans	Aspergius Niger
1	B-1	250	-	-
		500	-	-
2	B-2	250	-	+
		500	+	-
3	B-3	250	-	-
		500	-	-
4	B-4	250	+	-
		500	-	-
5	B-5	250	-	+
		500	+	-
6	Fluconazole	250	-	-
		500	-	-

Note: (-) No growth, (+) Growth,

Table no: 8-Anti-fungal activity data of synthesized Compound (A1-A5):

Sr.No	Compound	Concentration µg/ml	Candida albicans	Aspergius Niger
1	A-1	250	-	-
		500	-	+
2	A-2	250	+	-
		500	+	-
3	A-3	250	-	-
		500	+	+
4	A-4	250	+	-
		500	-	-
5	A-5	250	-	+
		500	+	-
6	Fluconazole	250	-	-
		500	-	-

Note: (-) No growth, (+) Growth

RESULTS & DISCUSSION:

All the reactions were monitored by TLC, structure and purity of the anticipated compounds were characterize by physical constant and FTIR spectral study. From the TLC we ensured to declare the completion of reaction. The TLC plates were visualized either by iodine vapors or by viewing in UV chamber. The reaction products of all the reactions were purified by different workup processes to remove unreacted starting material if any and recrystallization using suitable solvents. From the literature survey it reveals that indole have been reported for number of pharmacological activities and some molecules have shown significant activities and some compounds shows moderate and good activities. The synthesized all Indole derivatives were screened for anti-bacterial activity using DMF as a solvent against the organisms, Staphyloccoccus aureus and E. coli. And Antifungal activity using Aspergilusniger and Candida albicans. By Cup plate method on nutrient agar media. The standard drug used was Ciprofloxacin for antibacterial and Fluconazole as standard for antifungal activity. The antimicrobial screening results presented on above table reveals that compounds **B-4, B-5**exhibited Good activity against S.aureus and E.coli, at 50 µg/ml, but at 100 µg/ml and other have shown moderate activity against *S.aureus, E.Coli*. The compounds **A-2, A-3** exhibited Good activity against *S.aureus* and *E.coli*, at 50 µg/ml, but at 100 µg/ml and other have shown moderate activity against *S.aureus, E.coli*. The same Compounds also screened for the anti-fungal activity against Candida albicans the compounds **B-1, B-2, A-2, A-3** and as per gilusniger the compound **B-3, A-2** Showed highest degree of inhibition at 250µg/ml and 500µg/ml compared with the standard drug Fluconazole. However, the activities shown by all the compounds tested were less than that of the standard.

CONCLUSION:

The objective of the present work is to synthesize some novel indole derivatives and to study their antibacterial, anti-fungal activity. As expected, Indole derivatives exhibited significant, good and moderately active antibacterial agents when compared with standard employed for comparison. From antifungal in which some are good and some are less active than standard employed for comparison. Therefore, further a detailed study of toxicity is necessary. All the reactions were monitored by TLC, structure and purity of the anticipated compounds were characterize by physical constant and FTIR spectral study. From the TLC we ensured to declare the completion of reaction. The TLC plates were visualized either by iodine vapors or by viewing in UV chamber. The reaction products of all the reactions were purified by different workup processes to remove un-reacted starting material if any and re-crystallization using suitable solvents. The synthesized all Indole derivatives were screened for anti-

bacterial activity using DMF as a solvent against the organisms, Staphyloccoccus aureus and E.coli. and Anti-fungal activity using *Aspergilus Niger* and *Candida albicans*. By Cup plate method on nutrient agar media. The standard drug used was Ciprofloxacin for anti-bacterial and Fluconazole as standard for anti-fungal activity. The anti-microbial screening results presented on above table reveals that compounds **B-4,B 5** exhibited Good activity against *S.aureus* and *E.coli*, at 50µg/ml, but at 100µg/ml and other haves how moderate activity against *S.aureus, E.Coli*. The compounds **A-2, A-3** exhibited Good activity against S.aureus us and E.coli, at 50µg/ml, but at 100µg/ml and other have shown moderate activity against *S.aureus, E.Coli*. The same Compounds also screened for the anti-fungal activity against Candida albicans the compounds **B-1, B-2, A-2, A-3** and *Aspergilus Niger* the compound **B-3, A-2** Showed highest degree of inhibition at 250µg/ml and 500µg/ml compared with the standard drug Fluconazole. However, the activities shown by all the compounds tested were less than that of the standard. There is no such a thing as completely safe drug. Drugs are powerful tools, which alter physiological processes for the better or for the worse. A society that wishes to benefit from them will not achieve all the benefits open to it, if it ignores the fact and seeks for impossible standards of harmlessness. Further the detailed structural activity relationship studies are required along with the molecular manipulation i.e. molecular modelling may give better drugs. Molecules prepared for the biological testing do not always turn out as potential new drugs, but may be intended to serve as models for evaluation of hypothesis.

REFERENCES:

1. Bergman J, Lindstrom JO and Tilstam U. The structure and properties of some indolic constituents in Couropitaguianensisaubl. Tetrahedron. 1985;41: 2879-81.
2. Nassar E. Synthesis (in vitro) Antitumor and antimicrobial activity and pyrimidine derivatives linked to indole moiety. J American Sci. 2010;6(8):463-471.
3. Ji-Taili, Zhi-Ping Lin and Cai-Tong lin. Studyon the conjugate addition of indole with 1,5- diaryl-1,4-pentadien-3-ones catalyzed $Alcl_3$ under ultrasonication. Indian J Chem. 2008;47B:283-290.
4. Joule JA and Mills K. Indoles: Reaction and synthesis. Heterocyclic chemistry. 4^{th} edition. Black well publishing house. 2004:324-50.
5. Panda S and Chowdary V, Synthesis of novel indolyl-pyrimidine Anti-infammatory, Antioxidant and Antibacterial agent. Indian J Pharm Sci. 2008;208-215.
6. Banu s, Manjula A, Lath Mary T and Ravi T. De Nova drug design and synthesis of certain indole derivatives and screening for their xanthine oxidase inhibitory activity. Int J Pharm Tech Res. 2010;2(4):2128-2138.
7. Pahari N, Saha D, Jain V and Jain B. Synthesis and evaluation of acute toxicity studies and analgesic

characters of some novel indole derivatives. Int J Pharm Sci. 2010;1(9):399- 408.

8. Rahman A and Forghaly A. Synthesis, reaction and antimicrobial activity of some new indolyl-1,3,4-oxadiazole triazole and pyrazole derivatives. J Chinese Chem Society. 2004; 51:147-156.
9. Donawade D, Raghu A and Godaginamath G. Synthesis and antimicrobial activity of some new 1-substituted-3-pyrrolyl aminocarbonyl/oxadiazo/triazolyl/5-methoxy-2- methyl indoles and benz [g] indole. Indian J. Chem. 2006;45B:689-696.
10. Panwar H, Verma R, Srivastava V and Kumar A. Synthesis of some substituted aretidinonyl and thiazolidinonyl-1,3,4- thiadiazino [6,5-b] indoles as prospective antimicrobial agent. Indian J Chem. 2006;45B:2099-2104.
11. Pathak V, Gupta R and Gupta N. synthesis and biological evaluation of some new -4-5- dihydro-3-(2-aryl-indol-3-yl)-5-(4-chlorophenyl)-N Phenyl pyrazoles. Indian J Chem. 2008;47B:1303-1307.
12. Reji A, Manju S and Rajasekharan K. Synthesis of bis(arylamino) thiazoloyl indoles as novel analogs of dendrodoine. Indian J Chem2010;49B:323-326.
13. Amir M, Javed S and Kumar H. Synthesis and biological evaluation of some 4-(1H-indol-3- yl)-6-phenyl-1,2,3,4-tetrahydropyrimidin-2-ones / thiones as potent anti-inflammatory agents. Acta Pharm. 2008; 58:467-477.
14. Sondhi SM, Jain S, Rani R and Kumar A. Microwave assisted synthesis of indole and furan derivatives possessing good anti-inflammatory and analgesic activity. Indian J Chem. 2007;46B:1848-1854.
15. Sujatha K, Perumal P and Muralidharan D. Synthesis analgesic and anti-inflammatory activity of bis(indolyl) Methanes. Indian J Chem. 2009;48B:267-272.