Heterocyclic compounds are those cyclic compounds in which one or more of the ring carbons are replaced by another atom. The non-carbon atoms in such rings are referred to as "heteroatoms". Such bicyclic heterocyclic compounds containing pyrrole ring with benzene ring fused to α,β-position are known as Indoles. Indole has a benzene ring and pyrrole ring sharing double bond. It is a heterocyclic system with 10 electrons from four double bonds and the lone pair from the nitrogen atom. Indole is a popular component of fragrances and the precursor to many pharmaceuticals. Indole is an important heterocyclic system because it is built into proteins in the form of amino acid tryptophen, because it is the basis of drugs like indomethacin and because it provides the skeleton of indole alkaloids—biologically active compounds from plants including strychnine.

And LSD Because of their vast pharmacological activities, indole and their derivatives are an important class of heterocycles and bioactive intermediates in the pharmaceutical industry and organic synthesis. Chemists are continuously developing simple and efficient synthetic protocols to synthesize indoles and their derivatives due to their excellent biological activities.

Index Terms—Bioactive Indoles, Heterocyclic System, Cytotoxic Activities.

I. INTRODUCTION

The indole ring has become an important structural requirement in many pharmaceutical drugs because of the structural diversity of biologically active indoles and their derivatives. Indole is a valuable compound which has become prominent in medicinal chemistry because of its various biological activities. Indole ring is present in various marine or terrestrial natural compounds, which have useful biological properties. In last few years it was reported that indole, its bioisosters and derivatives had antimicrobial activity against gramnegative, grampositive bacteria and yeast candida albicans antimicrobial activity especially against Entero-bacter, Pseudomonas aeruginosa, E.Coli and staphylococcus epidermises.

A large number of efforts were made to synthesize different heterocyclic compounds and their derivatives in the past decade and were found to possess promising antitumor, anticonvulsant, antimicrobial anti tubercular and anti diabetic activities. Although indole moiety is very small but is fascinated by scientists because of the diverse biological activities by not only indole but its various substituted derivatives as well. This revisers is focused on the indole and its derivatives that are now in development. Due to its winder applications is pharmaceutical industries, they will replace many existing heterocyclic based pharmaceuticals.

Indole derivatives including bromoindoles have been isolated from the south pacific marine sponges Rhopalocides odorabile and Hyrtion sp. their potential inhibitory phospholipase A2 (PLA2), antioxidant and cytotoxic activities were evaluated.

A great variety of simple and substituted indole derivatives, including halogenated indoles, bisindoles and tryptamine derivatives, have been previously isolated from marine organism. Indole derivatives are known to display various bioactivities such as anticancer antibiotics and anti infatuatedly activities. Antioxidant activities were also recently reported for some analogues such as 2,2-diphenyl 1-picrylhydrazyl (DPPH) radical scavengers, highlighting an additional bioactivity is the series.

Indole derivatives possess a large number of biological activities.

II. ANTFUNGAL ACTIVITY

Some of the isatin and indole oximes synthesized by Abele et al. were found to be exhibiting high fungicidal activity where the oxime derivates of 2-substituted indoles (1) and 3-substituted indoles (2) demonstrated significant antifungal activity.

\[
\text{R,R'} = \text{Alkyl} \\
\text{R"} = \text{OAlk, SAlk, NHAlk, NAlk}
\]

(1)

(2)

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Dr. Meenakshi Jain, Dinesh Verma
A series of S-(indolyl-3)diethyl dithiocarbamates was synthesized and evaluated for their activity by Skii et al. The compounds were found to be exhibiting highest antifungal activity.

\[3a: R_1 = R_2 = H \quad 3b: R = H, R_1 = CH_2Ph \quad 3c: R = R_2 = H, R_1 = Ph\]

Many indole derivatives are reported as antifungal agents. Varma et al. have prepared some 2-indolinone derivatives (4) as active against some fungi species viz; Candida albicans Cryptococcus neoformans, Sporotricium schenckii, Trichophyton mentagrophytes and Aspergillus flumigatus.

Antifungal screening of Spiro[1,5]-benzothiazepin-2,3‘[3H] indol-2[1'H]-ones (5) has been done by Dandia et al. Kidwai et al. have reported novel antifungal indolyl (thio) barbituric acid derivatives (7)

Pathak et al. have also reported various indolyl derivatives useful as antifungal agent. Two indolyl alkaloids (8) (9) exhibit antifungal activities.

Various other indole derivatives have been reported as antifungal agents.

III. ANTIMICROBIAL ACTIVITY

The synthesis and antibacterial activity of some substituted 3-(aryl) and 3-(hetero-aryl) indoles were reported by Hiari et al. The most active compound was reported to be 3-(4-trifluoromethyl-2-nitrophenyl) indole (10) exhibiting MIC \( \approx 7 \mu g/cm^3 \) against Escherichia coli and Staphylococcus aureus.
Panwar et al. synthesis substituted azetidonyl and thia-zolidinonyl-1,3,4-thiadiazino[6,5-b] indoles as prospective antimicrobial agents. The compounds (11) and (12) were found to exhibit most inhibitory effect against *E. coli* and *S. aureus.*

Elkhayat et al. have reported 5-hydroxy-1H-indole-3-carbaldehyde (13) as antibacterial agent against *Bacillus subtilis.*

Pathak et al. have synthesized various indole derivatives that show promising antibacterial activity. These are *N*-(un)alkylated-2-arylindol-3(-yl)-thiocarboxamides (14), 1-butyl-3-substituted-4-(2-aryl-1H-indol-3-yl)-2-azetidinones (15), -aryl-1-(2-aryl-1H-indol-3-yl)prop-2-in-1-one (16) and 5-nitro-2-aryl-1H-indole-3-carboxaldehydes

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Some bis-indolyl derivatives (21), (22) also show antibacterial activities.
A large number of indole derivatives exhibit antibacterial activity.\textsuperscript{40-46} Various quinolinylindole derivatives\textsuperscript{47-49} are reported as active antibacterial agent. Gadaginamath \textit{et al.}\textsuperscript{12} have reported some 4,6-dinitroindole derivatives (23) as antibacterial agents.

3. Insecticidal activity, Sharma \textit{et al.} investigated the insecticidal activity of synthesized novel indole derivatives. The compounds (24) and (25) exhibited promising results against spodoptera liture (eighth instar larvae and Jeliothis armigera)\textsuperscript{50}.

IV. ANTICANCER ACTIVITY

The series of various tricyclic and tetra cyclic indoles synthesized by Hong \textit{et al.} were evaluated for their anticancer activity where the compounds 26,27,28, and 29 were found in exhibit highest in vitro activity against human nasopharyngeal carcinoma (HONE-1) and gastric adenocarcinoma (NUGC-3) cell lines.\textsuperscript{51}

Garcia \textit{et al.} synthesized pyrrolo [2,3-e] indole derivatives and evaluated them for possible in vitro cytotoxic activity. The most active compound was found to be (31), which shows best result in PC-3 (prostate) cell line\textsuperscript{52}.

A series of halogenated indole-3-acetic acids as oxidatively activated prodrugs with potential for targeted cancer therapy were reported by Rossiter \textit{et al.} These derivatives were oxidized by horse radish peroxidase (HRP) and toxicity against V79 Chinese hamster lung fibroblasts was
determined and the compound (32) was found to possess highest cytotoxicity and it was the best drug for targeted cancer therapy.\textsuperscript{53}

\[
\text{(32)}
\]

Queiroz et al. studied the inhibitory activity of the heteroarylindoles and of the phenylbenzothienoindole on the growth of human tumor cell lines, MCF-7 (breast adenocarcinoma), NCI-H460 (non-small cell lung cancer), and SF-268 (CNS cancer). The results showed that the methyl 3-(dibenzothen-4-yl)indole-2-carboxylate (33) had most potent growth inhibitory activity in all the tumor cell lines tested (with GI50 values ranging from 11 to 17 µM)\textsuperscript{54}

\[
\text{(33)}
\]

Anticancer activity\textsuperscript{55-63} is associated with a wide number of indole and allied compounds. Akayama et al.\textsuperscript{64} have prepared some indole derivatives as enhancers for activity of anticancer agents. Preparation of indolocarbazole derivatives\textsuperscript{65} (34 & 35) have been reported to treat prostatic cancer and hypertrophy.

\[
\text{(34)}
\]
\[
\text{(35)}
\]

\[
R = \text{OH, alkoxy, acyloxy}
\]
\[
R^1, R^2, R^3, R^4 = \text{H, Cl, F, Br, I, NO}_2, (N, \text{substituted ureido})
\]
\[
X = \text{H, CONHPh}
\]
\[
Z^1, Z^2 = \text{H, O (when combined)}
\]
\[
R^5, R^6 = \text{H, alkyl, hydroxyalkyl alkenyl}
\]

3-Methylenoxindole derivatives (36) are potential for use in cancer therapy.\textsuperscript{66}

\[
\text{(36)}
\]

The active components of indole-3-carbinol (I3C) have been used by Chao et al.\textsuperscript{67} to develop a novel class of indole analogs to optimize I3C’s anticancer actions. The most promising of these analogs, SR 13668 (37) exhibited potent oral anticancer activity against various cancers.

\[
\text{(37)}
\]

Antiviral activity. The indol oxime, carbamoyl derivative of indole-3-oxime (38) exhibited the most potent antiviral activity among the isatin and indole ximes synthesized by Abele et al.\textsuperscript{68}

\[
\text{(38)}
\]

Some indole derivatives are reported as inhibitors of HIV reverse transcriptase, which are useful in the treatment of AIDS. Slater et al. have reported synthesis of some N-alkyl substituted indolocarbazoles (39)as potent inhibitors of human cytomegalovirus replication. Regina et al. have reported some indolyl aryl sulfones bearing 5-chloro-4-fluoro substitution pattern at the indole ring (40). They were potent inhibitors of HIV-1 WT and the NNRTI-resistant strains Y181C and K103N-Y181C.
A few series of indole derivatives have been screened for antiviral activities by Olgen et al.\textsuperscript{73} Shi et al.\textsuperscript{74} have reported that Arbidol, ethyl-6-bromo-4-[(dimethylamino)-methyl]-5-hydroxy-1-methyl-2-[(phenylthio)methyl]-indole-3-carboxylate hydrochloride monohydrate is an antiviral chemical agent. They have studied the antiviral activity of arbidol against influenza A virus, respiratory syncytial virus, rhino virus, coxsackie virus and adenovirus in vitro and in vivo. A series of chlorinated indole nucleosides has been synthesized and tested for activity against human cytomegalovirus (HCMV) and herpes simplex virus type 1 (HSV-1) by Williams et al.\textsuperscript{2'5'} deoxy derivatives of the reported indole had been found as potent antiviral agent.

Varma et al.\textsuperscript{45} have prepared some indole derivatives useful as antiviral agents. Some indole derivatives\textsuperscript{40-76} have been reported as active against Herpes virus. Some antiviral indole derivatives (41) have been synthesized by Zatova et al.\textsuperscript{77}

Some indole derivatives have been synthesized which are useful in the treatment of diabetes insipidus. Dodd et al.\textsuperscript{81} have prepared some indole derivatives for treatment of diabetes mellitus. Yamgade et al.\textsuperscript{82} have prepared indole derivatives (43) as potent antidiabetic agents.

A series of substituted 3-benzyl-2-methyldiones, a subset of which were selective PPAR\(\gamma\) modulators (SPPAR\(\gamma\)Ms) (44) has been synthesized by ActonIII et al.\textsuperscript{83} SPPAR\(\gamma\)M have displayed robust anti-diabetic activity with an improved therapeutic window.

Some of the indole derivatives were evaluated for their insulin sensitizing and glucose lowering effects by Li et al. The indole derivative (42) showed increase in activity of PPAR\(\gamma\) agents, which shows decrease serum glucose and contributing to anti-diabetic activity.

Synthesis of bisindoly1quinone (45) natural product demethylasterriquinone B1 (also known as L-783,281) have been accomplished by Pirrung et al.\textsuperscript{84} and have been screened for their antidiabetic activity. 2-aryl-N-acylindole derivatives (46) have also been reported as potent antidiabetic agent by Kher et al.
Yadav et al. have also reported 3-indolyl quinones as potent antidiabetic agent.

Antituberculosis activity. A new series of 1H-indole-2,3-dione derivatives were synthesized and evaluated for in vitro antituberculosis activity against Mycobacterium tuberculosis H 37 Rv by Karali et al. Among the tested compounds, 5-nitro-1H-indole-2,3-dione-3-thiosemicarbazones and its 1-morpholonomethyl (47, 48, 49 and 50) derivatives exhibited significant inhibitory activity with MIC values ≥ 75%. Karali et al. synthesized and evaluated a new series of indole-2,3-dione derivatives and found that derivatives (52) and (53) have strongest scavenging effect on OH radicals, i.e., quenching > 30% and the derivatives (53) and (54) have strongest effect on scavenging of superoxide radicals.

VI. ANTIOXIDANT ACTIVITY

A series of indole derivatives were synthesized and biologically evaluated by Enien et al., and found that Indole-2 and 3-carboxamides were having antioxidant properties by Chemoluminescence and Electron spin resonance spin trapping. They further reported that the derivatives (52) and (53) have strongest scavenging effect on OH radicals, i.e., quenching > 30% and the derivatives (53) and (54) have strongest effect on scavenging of superoxide radicals.

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VII. CARDIOVASCULAR ACTIVITY

The isatin oxime (58) exhibited the highest antiarhythmic activity among the isatin and indole oximes synthesized by Abele et al. \(^{68}\)

\[
\begin{align*}
(58) \quad R &= H, \text{ Alkyl, OH, Halogen, NO}_2, \text{ NH}_2 \\
R &= H, \quad \text{ Halogen, OH SH NH}_2 \\
R_2 &= H, \text{ Alkyl, Ar} \\
R_3 &= H
\end{align*}
\]

A number of benzopyranyl indoline and indole analogs were synthesized and evaluated for Cardioselective anti-ischemic ATP-sensitive potassium channel (K\(_{\text{ATP}}\)) opener activity by Lee et al. The compounds (59) and (60) showed the best cardioprotective activity. \(^{92}\)

\[
(59) \quad (2-\text{S, 3-R, 4-S, 2-S}) = R = \text{Ethyl} \\
(60) \quad (2-\text{R, 3-S, 4-R, 2-R}) = R = \text{Ethyl}
\]

**Plant growth regulator.** The 3-substituted indole (61) was reported to be a plant growth regulator by Abele et al. among the various isatin and indole oximes synthesized and evaluated by them. \(^{68}\)

\[
(61)
\]

VIII. ANTIHYPERTENSIVE ACTIVITY

Among the various isatin and indole oximes reported by Abele et al., \(^{68}\) compound, (62), a tetracyclic derivatives of indole oximes, was found to have hypotensive activity lowering the blood pressure in rats by 28%.

\[
\begin{align*}
62 \quad \text{H}
\end{align*}
\]

IX. ANTIHISTAMINIC ACTIVITY

A number of indole amide derivatives bearing a side chain, in which the indole ring replaces the isoster benzimidazole nucleus typical of some well known antihistamines, were prepared and tested for the antihistaminic activity by Battaglia et al. The most active compounds (63 64 66 67) and (68) were tested in vivo for their ability to antagonize histamine induced cutaneous vascular permeability in rats. \(^{93}\)

<table>
<thead>
<tr>
<th>Compound no.</th>
<th>(R_1)</th>
<th>(R_2)</th>
<th>(R_2)N-R_3</th>
</tr>
</thead>
<tbody>
<tr>
<td>63</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_5)</td>
<td>(\text{CH}_3)CH _3</td>
</tr>
<tr>
<td>64</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_5)</td>
<td>Piperidine</td>
</tr>
<tr>
<td>65</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_4\text{p-F})</td>
<td>(\text{CH}_3)CH _3</td>
</tr>
<tr>
<td>66</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_4\text{p-F})</td>
<td>Piperidine</td>
</tr>
<tr>
<td>67</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_4\text{p-Cl})</td>
<td>(\text{CH}_3)CH _3</td>
</tr>
<tr>
<td>68</td>
<td>H</td>
<td>(\text{CH}_2\text{C}_6\text{H}_4\text{p-Cl})</td>
<td>Piperidine</td>
</tr>
</tbody>
</table>

**Opioid antagonist.** The synthesis and biological activity of 8β-substituted hydromorphone indole derivatives were carried out by Yu et al. The compound, 6,7-dehydro-4,5α-epoxy-8β-methyl-6, 7,2',3'-indolomorphinan (69) was found to be a δ antagonist with submolar affinity (0.7 nM) for the opioid receptor, and to have good δ-selectivity (\(\mu/\delta = 322\) nM). \(^{94}\)

\[
(69)
\]
X. PHOTOCHEMOTHERAPEUTIC ACTIVITY

The synthesis and photochemotherapeutic activity of thiopyrano [2,3-e] indol-2-ones was performed by Barraja et al., wherein the compound thiopyrano [2,3-e]-indol-2-ones (70) showed the maximum photoxicity on two cultured cell lines: HL-60 and LoVo.

XI. ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY

Abele et al. synthesized is at in and indole oximes and carried out the chemical reactions and biological activities of the synthesized compounds where the compound (71) was found to be the most active analgesic and anti-inflammatory agent.

Radwan et al. carried out the synthesis and biological evaluation of 3-substituted indole derivatives as potential anti-inflammatory and analgesic agents. They reported 3-(3-indolyl) thiophene derivative (72) as a potent anti-inflammatory compound whereas thiazolidine-4-one derivative (73) exhibits analgesic activity.

Kalaskar et al. synthesized indole-3-acetic acids and evaluated them for their in vivo anti-inflammatory activity. The compound 1,2-disubstituted-5-methoxyindole/benz(g) indole-3-acetic acid (74) showed significant activity.

The synthesis and anti-inflammatory activity of heterocyclic indole derivatives was performed by Rani et al. The compound (75) was found to be the most potent (inhibition of oedema at 50 μg/Kg dose).

Amir et al. carried out synthesis and anti-inflammatory activity on various indole and indazole derivatives where the compounds 2-Phenyl-3-(2'-carboxyphenyliminomethyl) indole (76) and 2-phenyl-3-(2'-carboxyphenyliminomethyl) indol-1-acetic acid (77) were found to be the most potent.

2-Benzoyl-3-dialkylamino-ethoxyindoles (78) have been screened for their anti-inflammatory activity by Brandstrom et al. Shen et al. have reported that Indomethacin (79) is one of the most potent nonsteroidal anti-inflammatory drug.
Various other acyl derivatives of indole (80) have been screened for anti-inflammatory activities by Henri et al.102. Some tetrazole derivatives of 2-phenyl-3-mercaptoindoles (81) have been reported to possess anti-inflammatory activity.103

R1=CH3, Ar
NR2=methylamino, dimethylamino, diethylamino, morpholino, piperidino
n=0, 1, 2

Sonar et al.104 have reported oxadiazolylindole derivatives (82) as potent anti-inflammatory agent.

Some other indole derivatives have also been found as a potent anti-inflammatory agent.105-108

Some pyrimido [4,5-b] indoles (83) have been screened for their anti-inflammatory activity by Zhang et al.108,109

A large number of indole derivatives exhibit anti-inflammatory activity.110-126 Structure-activity studies of 4,6-disubstituted-2-(morpholinocarbonel) fur [3,2-b] indole derivatives127 with anti-inflammatory activity have been reported. Andreani et al.128 have reported the synthesis and anti-inflammatory activity of some indolylacrylic acids (84).

Sonar et al.104 have reported oxadiazolylindole derivatives (82) as potent anti-inflammatory agent.

Some fluorine containing 2,3-bis (4-methoxyphenyl) indole and related compounds (86) are potent analgesic.133,134

Some other indole derivatives have also been found as a potent anti-inflammatory agent.105-108

Some pyrimido [4,5-b] indoles (83) have been screened for their anti-inflammatory activity by Zhang et al.108,109

A number of indole derivatives (87) have been synthesized and screened for their analgesic activity by Sondhi et al.135

Novel 3-(4-piperidinylthio)-1H-indoles136 have been reported as potent nonopioid orally active central analgesic and (indol-3-yl) alkylamides137 have also been reported as potent analgesic agents.
XII. ANTIDEPRESSANT, TRANQUILLIZING, AND ANTICONVULSANT ACTIVITY.

The oxime of indole aminoketone (88) exhibited high antidepressant activity among the isatin and indole oximes synthesized and evaluated for their biological activity by Abele et al.68

\[
R = H, R' = H, \text{methyl } R'' = \text{methyl, ethyl } R''' = H, \text{Cl, OMe}
\]

A series of N-substituted indoles were synthesized by Falco et al., and afterwards, in vitro screening and in vivo spontaneous motor activity in mice had revealed molecules with good in vitro affinities for the \(\alpha_1\)-subunit of GABA\(_A\) receptor and potent in vivo induction of sedation and (89) was found most potent compounds138.

\[
(88)
\]

\[
R = H, R_1 = H, \text{methyl } R'' = \text{methyl, ethyl } R''' = H, \text{Cl, OMe}
\]

Clawson et al.142 have also prepared some pyrano [3,2-b] indoles (92) as antiallergics.

\[
(91)
\]

\[
R_1 = R_2 = \text{methyl, } R_3 = \text{propyl}
\]

Clawson et al.142 have also prepared some pyrano [3,2-b] indoles (92) as antiallergics.

\[
(92)
\]

Shigenaga et al.143 have reported synthesis and antiallergic activity of (2E,4E)-N-{4-(1H-indol-3-yl) piperidine-1-yl} alkyl-5-(substituted phenyl)-2,4-pentadienamides.

LXR receptor agonist. A series of 2-Aryl-N-acyl indole derivatives was synthesized and biologically evaluated as liver X receptor (LXR) agonists by Kher et al. The compound (93) was found to be most active with \(EC_{50}=0.012\mu M\)144.

\[
(93)
\]

R_1 = \text{COPh, } R_2 = (\text{CH}_2)_2\text{CN}

ACAT inhibitors (hypocholesterolic activity). The indole derivatives synthesized by Bellemin et al., were evaluated for their hypocholesterolic activity. The compounds (94) (95) were found to be most effective ACAT inhibitor with \(ED_{25}\) values of 0.098 and 0.063 mg/Kg, respectively145.

\[
(94): R_1 = \text{CH}_3, R_2 = H, R_3 = R_4 = (\text{CH}_2)_3, R_5 = 2,6-(\text{i-Pr})_2\text{C}_6\text{H}_3
\]

\[
(95): R_1 = (\text{CH}_2)_2\text{N}(\text{CH}_3), R_2 = H, R_3 = R_4 = (\text{CH}_2)_3, R_5 = 2,6-(\text{i-Pr})_2\text{C}_6\text{H}_3
\]

Galanine GAL\(_3\) receptor antagonist. A series of 3-arylimino-2-indolones were reported to be as Galanine
GAL₂ receptor antagonists by Konkel et al. The compound (96) was found to be most potent antagonist with \( K_b = 29 \text{ nM}^{46} \).

![Image of compound 96](image)

XIV. ANTI-OBESITY ACTIVITY

Various indole derivatives have been prepared which are useful in the treatment of obesity\(^80,82,147-149\). Adams et al.\(^80\) have reported the preparation of pyrroloindoles, pyridoindoles and azepinoindoles (97) as antiobesity agents.

![Image of compound 97](image)

Indolopyridoquinazolinone alkaloid (Rutaecarpine) (98) has been reported as a potent antiobesity agent by Lee et al.\(^85\). Li et al.\(^150\) have reported in vitro and in vivo profile of 5-[(4'-trifluoromethylbiphenyl-2-carbonyl)-amino]-1H-indole-2-carboxylic acid benzylmethyl carbamoylamide (dirlotapide) (99) as a novel potent MTP inhibitor for obesity.

![Image of compound 99](image)

Selective CB2 receptor agonist. The preparation and evaluation of a class of CB2 receptor agonist based on a 1,2,3,4-tetrahydropyrrrolo [3,4-b] indole moiety were reported by Page at al. The compound (100) showed to be most potent CB2 receptor agonist.\(^151\)

![Image of compound 100](image)

IL-1 inhibitors. Amongst the series of hydroxyindole derivatives synthesized and evaluated for IL-1 generation inhibitors by Tanaka et al., the compound (101) was found to be potent inhibitors of IL-1 generation with IL-1α=6.4 \( \mu \text{M} \) and IL-2 = 8.6 \( \mu \text{M}^{152} \).

![Image of compound 101](image)

\( \text{LTB}_4 \) production inhibitor. The compounds (102) and (103) exhibited the highest inhibitory activity against \( \text{LTB}_4 \) production among the series of novel thiopyrano [3,2-b] and cycloalkeno [1,2-b] indole derivatives synthesized and evaluated by Caubere et al.\(^153\).
Steroid 5α-reductase inhibitor. A class of indole and benzimidazole derivatives were synthesized and evaluated for their inhibitory activity against rat prostatic 5α-reductase by Takami et al. The compounds (104) and (105) were found to be showing most potent inhibitory activity against rat prostatic 5α-reductase with IC$_{50}$ = 9.6 ± 1.0 nM and 19 ± 6.2 nM, respectively$^{154}$.

**Glycoprotein IIb/IIIa inhibitors.** Grumel et al, synthesis 1,3-disubstituted indole derivatives as glycoprotein IIb/IIIa antagonists wherein the compound (106) was found to exhibit highest Glycoprotein IIb/IIIa inhibitory activity with IC$_{50}$ = 4.5 μM$^{155}$.

**Thrombin catalytic activity.** The substituted 5-amide indoles were evaluated as inhibitors of thrombin catalytic activity by Iwanowicz et al. The compound (107) was found to be the most potent inhibitor of thrombin catalytic activity with an inhibition constant, K$_i$ = 260 nM$^{156}$.

**Peroxisome proliferator-activated receptor agonist.** A series of indole based PPAR agonist were synthesized and biologically evaluated by Mahindroo et al.$^{157}$ The compound (108) was found to be most potent PPAR agonist with IC$_{50}$ = 0.050μM and EC$_{50}$ = 0.070μM.

**Cytosolic phospholipase A2α inhibitors.**

**A. Cytosolic phospholipase A2α inhibitors.** The potential of indole nucleus as Cytosolic Phospholipase A2α inhibitors was evaluated by Mckew et al. the compound (109) was found to be most potent IC$_{50}$ = 0.5μM in the rat whole blood assay$^{158}$.

**B. Galanine GAL$_3$ receptor antagonist**

Selective dopamine agonist. A Series of 2-(aminomethyl)-3,4,7,9-tetrahydro-2H-pyran[2,3-e] indole and indole-8-one derivatives were synthesized and evaluated by Mewshaw et al. The compound (110) was found to be most potent agonist$^{159}$. 

---

(102) R=2-quinyl

(103) R= 2-quinolyl

(104) R$_1$ = 4, 4′ – dipropylbenzhydryl

(105) R$_1$ = 4-isobutyl-α-methylbenzyl

(106) R=H, HCl

(107)

(108) Y=n-Proply

(109) X=SO$_2$
The class of cis- and trans-2,3,3a,4,5,9b-hexahydro-1H-binz[e] indoles synthesized by Song et al. were evaluated for dopamine D₂ and D₃ receptor binding affinity. The cis-diastereoisomer (111) was found to be more potent among the synthesized compounds.

Antifertility activity

Some indole and allied derivatives have been found to act as effective antifertility agents. Some new fluorine containing 2-[(2-(fluoroaryl)-1H-indol-3-yl) methylene] hydrazine carbothioamides and 2-(fluoroaryl)-[5-(substituted benzylidene)-4-oxo-2-thiazolidinylidene] hydrazone]-1H-indole-3-carboxaldehydes (112) have been prepared for possible antifertility activity.

Antitumor activity

Antitumor activity is exhibited by many indole derivatives. The preparation and antitumor activity in human ovarian carcinoma cell line, of chloro-substituted-3-triarylmethyl indoles have been described by Skurydina et al. Maeda et al. have prepared some bis-indole derivatives (113) as antitumor agents.

A number of 2-phenylindole derivatives (56) have been synthesized and screened for their antitumor activity by Angerer et al. Mohamed et al. have reported synthesis and antitumor activity of indolylpyrimidines (114).

Dong et al. have also reported synthesis and antitumor activity of 1-indole substituted beta-carboline alkaloid and its derivatives.

CNS activity

A large number of indole and allied derivatives act as CNS affecting agents. Some indole derivatives possess antidepressant activity and antianxiety (anxiolytic) and memory enhancing activities. Various indole derivatives have been synthesized as antipsychotic, neuroleptic, antimanic and anticonvulsant drugs. Preparation and neurotropic activity of 4-oxo-3,5-dihydro-4H-pyridazino-[4,5-b]indole-1-carboxamides (115) have been reported by Margnet et al.
X=H, halo; Y=H, halo, Me, OMe, NO₂
R₁=C₄alkyl; R₂=R₃=H, C₁-C₄ alkyl
R₂NR₃= pyrrolidinyl, piperidinyl, morpholinyl

Mewshaw and Webb²⁰¹ have prepared 4-(2-aminoethoxy)-indoles (116) for treatment of Schizophrenia.

R₁, R₂, R₃= H or CH₃; R₄= H, CH₃, OCH₃

Some other indole derivatives have also been reported as hypotensive agents²⁰⁶-²¹₃

Serotonin (5th) antagonist activity
Antagonism of serotonin¹³⁹,¹⁴¹,¹⁷⁷,¹⁷⁹,¹⁸⁸,¹⁸⁹,²¹⁴-²²⁷ is exhibited by a wide number of indole derivatives. Bermudez et al²²⁸ have synthesized 1-indolinecarboxamides (120) as 5-HT₃ receptor antagonists.

X=NH, O
R₁= Me, Et
R₂= H, F, Cl, MeO, NO₂
R₃= H, Me, Et, Ph etc.
R₄= H, Me etc.
R₅= H, Me
n=1-3

Some 2,3-dialkyl (dimethylamino) indoles²²⁹ have been reported as potent antagonists of 5-HT₁ and 5-HT₂ receptors. A series of 3-substituted-1-(4-fluorophenyl)-1H-indoles (121) have been reported as 5-HT₂ antagonists by Perregaard et al²³⁰.

n=2-6
R= H, Me, Ph, isoropyl, cyclopentyl

Some bisindolyl derivatives like 1,4-bis(2-indol-3-yl-ethyl) piperazines (119) display antihypertensive activity²⁰⁵.

4-(Aminoalkyl)-2-indolinone derivatives²⁰⁴ (118) have been synthesized as hypotensive agents.
Rowley et al.\textsuperscript{232} and Kato et al.\textsuperscript{233} have also reported some serotonin antagonists. 

**Serotonin (5-hydroxytryptamine) receptor activity**

Some indole and allied compounds also act as serotonin (5-HT) receptor ligands. Fernandez et al.\textsuperscript{234} have prepared some hexahydrocarbazoles (123) and spiroindoles (124) as 5-HT\textsubscript{2A} serotonin receptors\textsuperscript{235-237}.

Ennis et al.\textsuperscript{235} have reported some 3,4,5,11a-hexahydro-1H-[1,4]diazepino[1,7-a] indoles (125) as new templates for 5-HT\textsubscript{2C} agonists.

Various other indole derivatives have also been reported as serotonin agonists\textsuperscript{238-240}.

**Lipoxygenase inhibitor.** Zheng et al. synthesized a series of indole derivatives as possible 5-lipoxygenase inhibitors. In all, four compounds (126.127.128.129) exhibited the most potent inhibitory activity with \( IC_{50} \) values ranging from 0.74 \( \mu \text{M} \) to 3.17 \( \mu \text{M} \)\textsuperscript{88}.

**HIV inhibitors.** The analogs of pyrimido [5,4-b] indoles were synthesized and biologically evaluated by Merino et al. for their possible HIV inhibitory activity. The derivative (130) formed by substitution at position 2 in analog-1 and derivative (131) at position 2,4 in analog II (formed in 65% and 64% maximum yield) were reported to be the inhibitors of wild and mutant HIV-1 RT types in an "in vitro" recombinant HIV-1 RT screening assay as well as anti-infectives in HLT4lacZ\textsubscript{1IIIB} cells\textsuperscript{89}.

**REFERENCES**
