

Exploring the Diverse Pharmacological Activities of Indole Derivatives-A Comprehensive Review

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Abstract:

This review explores the pharmacological properties of indole derivatives across diverse medical domains. Investigating antidiabetic, anti-inflammatory, anticonvulsant, anticancer, antimalarial, antitubercular, antioxidant, and antidepressant activities, the study reveals promising results. Noteworthy findings include potent antidiabetic effects in animal models, superior anti-inflammatory properties, and potent compounds for anticonvulsant and anticancer activities. Indole derivatives also exhibit significant potential against malaria and tuberculosis. Additionally, their antioxidant and antidepressant activities demonstrate therapeutic promise. This comprehensive overview underscores the potential of indole derivatives as versatile candidates for drug development across various therapeutic areas.

Keywords: Indole derivatives, Antidiabetic, Anti-inflammatory, anticonvulsant, Anticancer, Drug development

1.INTRODUCTION:

Indole, a bicyclic aromatic heterocycle derived from pyrrole, has garnered substantial attention in the realm of medicinal chemistry owing to its remarkable biological activities and versatile pharmacological properties [1,2]. Its distinctive structural motif, characterized by a benzene ring fused to a pyrrole ring, imparts unique chemical reactivity and a diverse array of interactions with biological macromolecules [3,4,5]. The chemistry of indole and its derivatives has been extensively explored, revealing a rich landscape of compounds with potent biological activities that span various therapeutic areas [6]. At the core of indole's significance lies its prevalence in natural products, playing a pivotal role in the molecular architecture of numerous bioactive compounds [7]. From the intricate structures of alkaloids to the sophisticated frameworks of certain hormones and neurotransmitters, indole serves as an indispensable building block in the intricate tapestry of bioorganic chemistry [8,9]. This pervasive presence underscores the evolutionary importance and functional versatility of indole in biological systems [10]. The biological activities of indole derivatives have been a subject of intense investigation, encompassing a broad spectrum of pharmacological effects [11,12]. Researchers have delved into the potential of indole derivatives as therapeutic agents in diverse areas, including antidiabetic, anti-inflammatory, anticonvulsant, anticancer,

antimalarial, antitubercular, antioxidant, and antidepressant activities [13,14,15]. This collective exploration has unveiled a myriad of promising compounds, each with its distinct pharmacological profile, offering avenues for targeted drug development and innovative treatment modalities [16]. In the context of antidiabetic activity, the synthesis and evaluation of novel indole derivatives have demonstrated encouraging results in preclinical models, showcasing their potential in addressing the global health challenge of diabetes [17]. The anti-inflammatory properties of indole derivatives have been elucidated through the inhibition of pro-inflammatory cytokines and key enzymes, suggesting therapeutic implications in conditions characterized by dysregulated immune responses [18,19]. Indole derivatives have also emerged as potent anticonvulsant agents, with studies identifying compounds surpassing standard drugs in mitigating seizures [20]. The anticancer potential of indole derivatives has been a focal point, revealing compounds with significant cytotoxic effects against diverse tumour cell lines, providing impetus for further investigations in oncology drug development. Furthermore, indole derivatives have exhibited remarkable antimalarial activity, presenting a promising avenue for combating one of the world's most significant infectious diseases [21,22]. In the domain of antitubercular activity, indole derivatives have demonstrated inhibitory effects against

Mycobacterium tuberculosis, contributing to the ongoing efforts to address the global burden of tuberculosis [23]. Indole derivatives exhibit significant antioxidant potential, countering free radicals and alleviating oxidative stress, thereby contributing to cellular defence mechanisms [24,25,26]. Additionally, these derivatives demonstrate promise in combating depression, displaying efficacy in preclinical models and suggesting new paths for psychotropic medication development [27]. This intersection of synthetic chemistry and pharmacology offers intriguing possibilities. The intricate relationship between molecular structure and pharmacological function underscores the potential of indole derivatives in inspiring therapeutically relevant compounds [28,29]. This review aims to offer a comprehensive overview of indole's contributions to medicinal chemistry, highlighting its diverse roles in addressing health challenges.

2. BIOLOGICAL ACTIVITIES OF INDOLE DERIVATIVES:

2.1 Antidiabetic Activity:

In 2018, Rajan and colleagues conducted a study on novel indole-triazole derivatives with potential antidiabetic properties. The research utilized the Syrian Golden Hamster model to evaluate the synthesized compounds, revealing that compound **1**, (Figure1) exhibited the highest potency among the tested compounds [30].

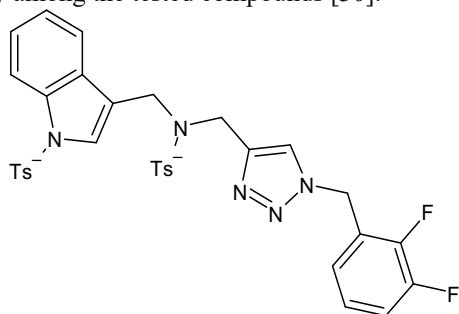


Figure: 1

Nazir et al. in 2018 focused on indole oxadiazole hybrids aimed at inhibiting α -glucosidase activity. Compounds **2** (figure2) ($IC_{50} = 9.46 \pm 0.03 \mu M$) and **3** ($IC_{50} = 9.37 \pm 0.03 \mu M$), demonstrated superior potency compared to the standard acarbose ($IC_{50} = 37.38 \pm 0.12 \mu M$). The evaluation utilized an in vivo study on a diabetes-induced chick model [31].

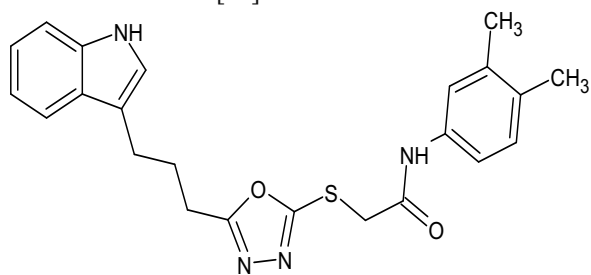


Figure :2

In a 2017 study, Srividya and Reddy investigated indole derivatives using a diabetes-induced chick model. Compound **3** (Figure3) (29.6-38.6%), exhibited noteworthy antidiabetic activity, surpassing the standard drug glipalamide (57.10%) [32].

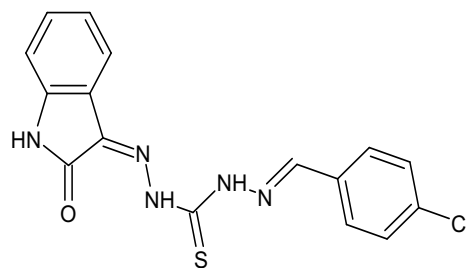
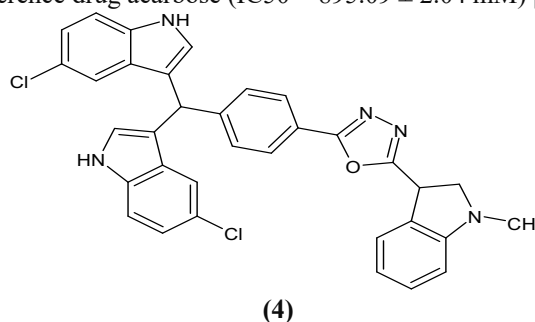
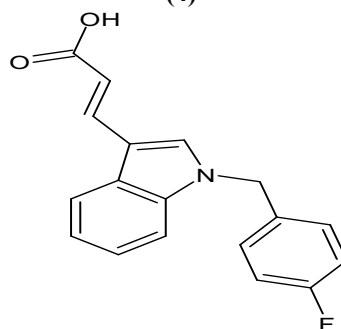


Figure:3

Taha et al. in 2017 developed a series of tris-indole-oxadiazole analogs by combining indole and oxadiazole. The synthesized compound **4**, **5**(Figure4) ($IC_{50} = 2.00 \pm 0.001 mM$), displayed higher potency compared to the reference drug acarbose ($IC_{50} = 895.09 \pm 2.04 mM$) [33].



(4)

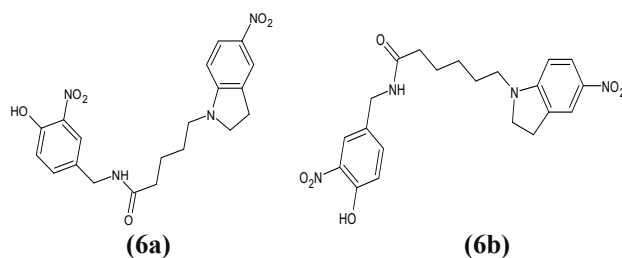


(5)

Figure: 4

2.2 Anti -Inflammatory Activity:

A Study conducted by Mukhtung et al. in 2018, derivatives of 1H-indole capsaicin and nitro-indole were synthesized and evaluated for their impact on the pro-inflammatory cytokine TNF- α . Among these derivatives, compound **6a** exhibited a 47.65% relative inhibition, while compound **6b** demonstrated a 51.95% relative inhibition. (Figure5) Notably, these compounds showed significant potency, although slightly lower than the standard drug capsaicin, which displayed a 65.55% relative inhibition [34].

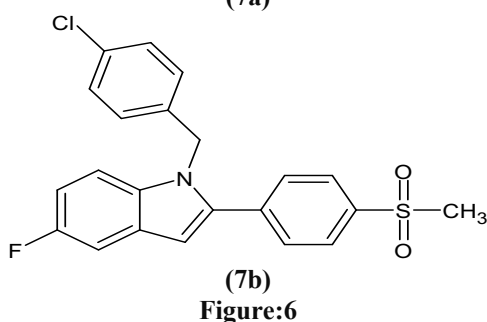
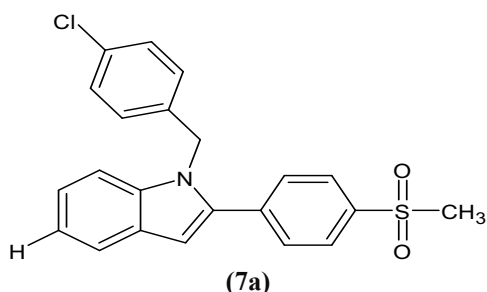


(6a)

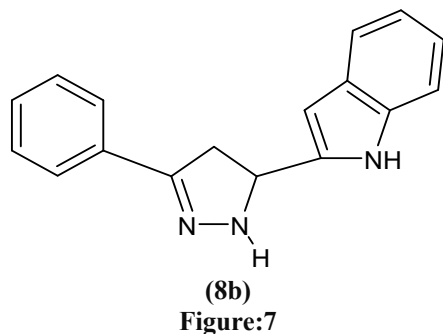
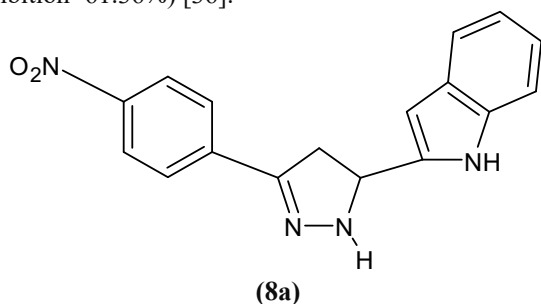
(6b)

Figure:5

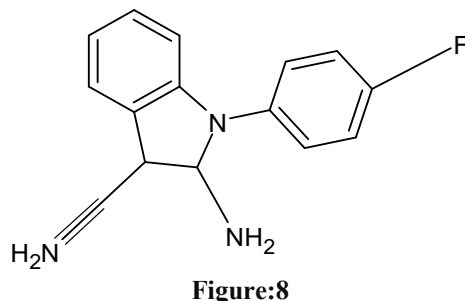
Additionally, Shaker et al. in the same year prepared and studied indole derivatives with methyl sulfonyl and aryl substitutions for COX-2 inhibition. Compounds **7a** and **7b** (Figure6) displayed higher potency ($IC_{50}=0.11 \mu M$, $SI=107.63$ and $IC_{50}=0.15 \mu M$, $SI=76.6$, respectively) compared to the reference drug indomethacin ($IC_{50}=0.49 \mu M$, $SI=0.079$) [35].



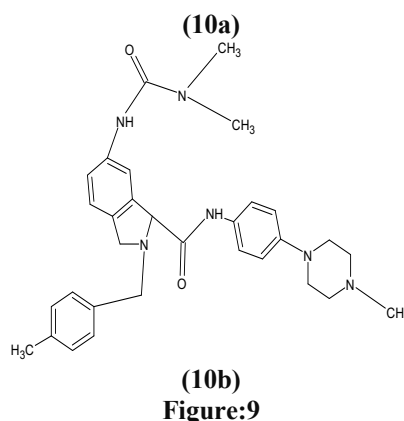
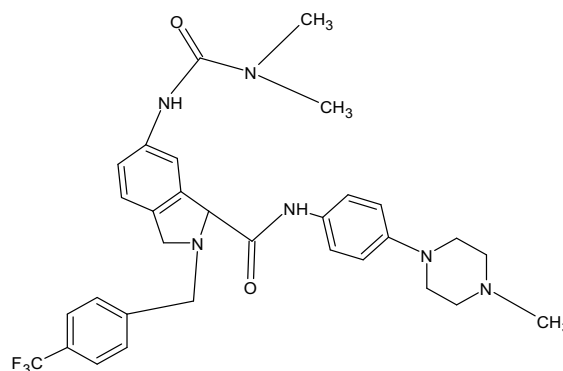
Moreover, novel indolyl-pyrazoline derivatives synthesized by Shroff and Daharwal in 2017 were evaluated for their anti-inflammatory properties using the Carrageenan-induced paw edema method. Compounds **8a** and **8b** (Figure7) exhibited superior potency (% of inhibition=63.90% and % of inhibition=57.46%, respectively) compared to indomethacin (% of inhibition=61.36%) [36].



In another study, Fatahala et al. (2017) investigated various indole derivatives for their anti-inflammatory properties using the paw edema method. Compound **9** (Figure8) demonstrated the highest potency with a % inhibition of 92%, surpassing ibuprofen (% of inhibition=69.84%) and indomethacin (% of inhibition=78.58%) [37].



Xu et al. (2019) conducted a study wherein they synthesized and evaluated indole-2-carboxamide derivatives for their potential as anti-inflammatory agents. Compounds **10a** and **10b** (Figure9) displayed promising potency (% of inhibition $< 2.90 \pm 0.73\%$ and % of inhibition $< 2.670.76\%$, respectively) [38].



Furthermore, Shaveta and colleagues (2014) synthesized chromone-substituted oxindole derivatives and tested them on COX-1, COX-2, and 5-LOX. Compounds **11a** and **11b** exhibited higher potency ($IC_{50} = 9.5 \pm 0.8 \mu g/mL$ and $IC_{50} = 10.0 \pm 4.2 \mu g/mL$, respectively) compared to indomethacin ($IC_{50} = 0.7 \pm 0.2 \mu g/mL$). The structures of the indole derivatives with anti-inflammatory activity (**11a-11b**) [39] (Figure10).

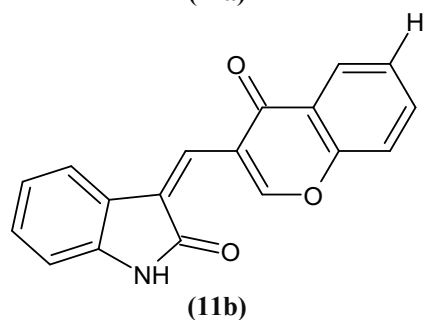
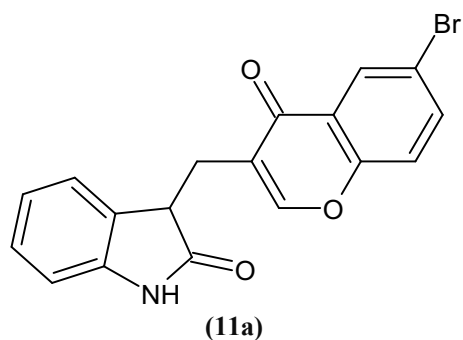


Figure:10

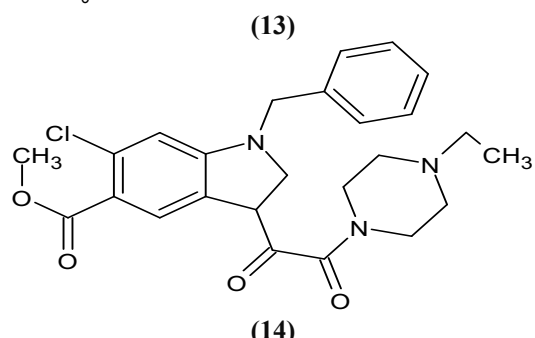
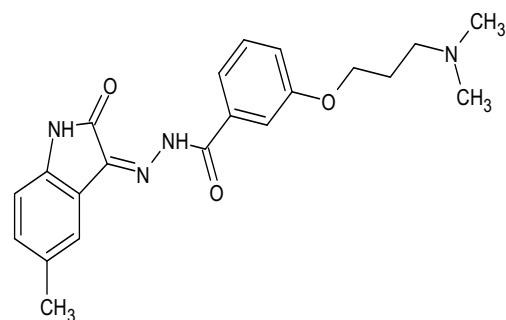


Figure:12

2.3 Anticonvulsant Activity:

In a study conducted by Swathi and Saragapani in 2017, dialkylamino alkoxy-oxindole analogs were synthesized and examined for their anticonvulsant activity using the pentylenetetrazole (PTZ) induced convulsion method and maximal electroshock seizure (MES). Compound 12 (Figure 11) displayed significant anticonvulsant activity with an IC₅₀ value below $67.18 \pm 0.23 \mu\text{g/mL}$, surpassing the efficacy of the standard drug Phenytoin [40].

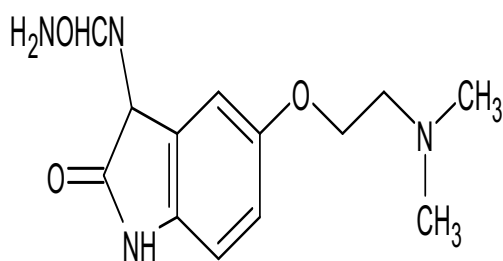


Figure:11

Madhira et al. (2017) focused on benzohydrazide-oxindole derivatives for anticonvulsant activity. Compound 13 exhibited higher potency, with a % protection of 83.19%, in comparison to the reference drug phenytoin (% protection=100%)⁴¹. Raju and colleagues (2016) investigated a novel indole carboxylate derivative for its anticonvulsant activity using the MES method. Compound 14 demonstrated superior potency (108.3 ± 0.7) compared to the reference drug phenytoin (100%) [42]. (Figure 12)

Ahuja and Siddiqui synthesized indole-1,2,4-triazine analogs and assessed their anticonvulsant activity against maximal electric shock (MES) and subcutaneous pentylenetetrazole (scPTZ). Compound 15 (Figure 13) with a % protection of 100%, exhibited enhanced potency, attributed to the presence of nitro groups interacting with the receptor [43].

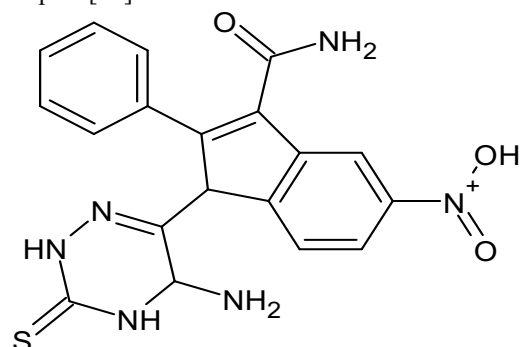


Figure:13

2.4 Anticancer activity:

Zhuang et al. conducted a study focusing on a series of 2,4-disubstituted furo indoles to assess their anticancer properties against the human NCI-60 tumour cell lines. Among the compounds tested, specifically compound 16 exhibited the most potent anticancer activity. The analysis of the results suggests that the molecular fingerprint of compound 16 (Figure 14) bears similarities to NSC-754549, indicating potential similarities in their mechanisms or modes of anticancer action [44].

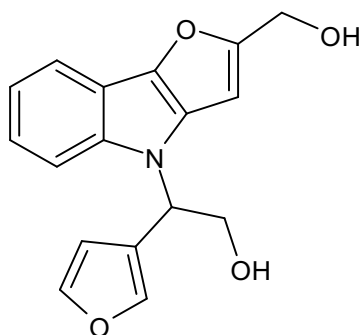


Figure:14

Gurkan-Alp et al. synthesized a series of novel (E)-3-(5-substituted-1H-indol-3-yl)-1-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl) prop-2-en-1-one derivatives and investigated their potential anticancer effects. Among these derivatives, compound **17**(Figure15) demonstrated the highest level of activity. This suggests that this specific compound has notable anticancer properties, as observed in the study conducted by Gurkan-Alp and colleagues [45].

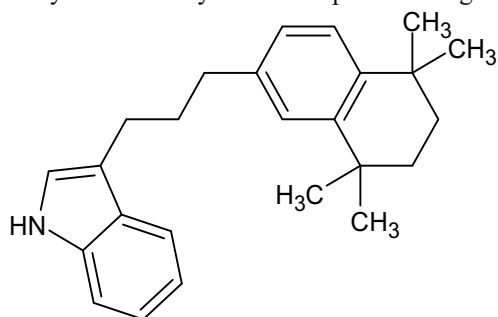


Figure:15

Indoles bearing 2,3-dimethyl substituents and tetrahydro carbazoles have exhibited notable anticancer efficacy against a range of cancer cell lines, such as MCF10A, Calu1, HCT116, Panc1, ACHN, and H460. This information is based on findings reported by Kumar et al., who employed a staining assay using propidium iodide (PI). Compounds such as 2,3-dimethyl-1H-indole (**18**) and 5-fluoro-2,3-dimethyl-1H-indole (**19**) (Figure16) were identified as cytotoxic agents against the mentioned cancer cell lines [46]. The observed cytotoxicity highlights the potential therapeutic value of these compounds in the treatment of cancer.

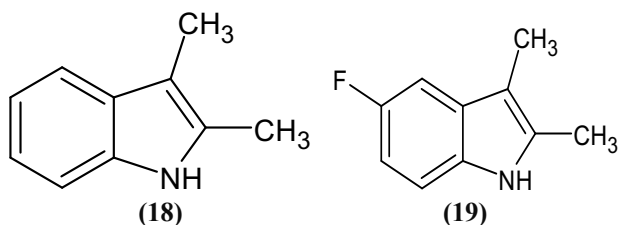


Figure:16

In a study conducted by Lafayette and colleagues in 2017, indole derivatives were synthesized and examined for their potential as DNA-binding sites with antitumor and anti-topoisomerase activity. Compound **20**, (Figure17) identified in their research, demonstrated significant

antitumor efficacy against T47D cell lines, with an IC₅₀ value of 1.93 μ M [47].

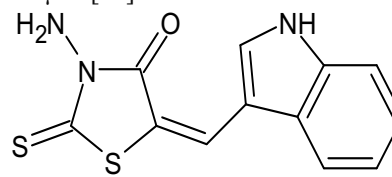


Figure:17

In a separate investigation by Chang et al. in 2016, a series of bis(hydroxymethyl)indolizing hybrids, consisting of β -carboline and bis(hydroxymethyl)pyrrole, were synthesized to assess their antitumor properties and their impact on lung cancer cells. Compound **21**(Figure 18) exhibited notable anticancer activity, with an IC₅₀ value of 0.49 μ M, surpassing the effectiveness of cisplatin (IC₅₀ = 0.63 μ M) in inhibiting the growth of small cell lung cancer (SCLC) H526 cells in xenograft [48].

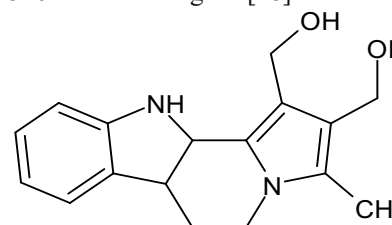


Figure:18

Furthermore, in 2019, Bakherad and colleagues investigated various thiosemicarbazone indole derivatives on MCF-7 (breast cancer), A-549 (lung cancer), and Hep-G2 (liver cancer) cell lines. Compound **22**(Figure19) demonstrated potent activity against A-549 (IC₅₀ = 12.5 μ M) and Hep-G2 (IC₅₀ = 56 \pm 6.30 μ M) cell lines, surpassing the efficacy of the reference drug etoposide on A-549 cells [49].

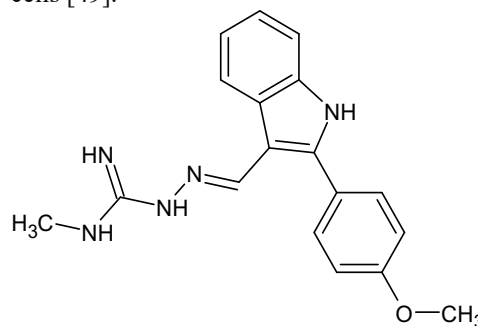


Figure:19

2.5 Antimalarial activity:

Elshehy and colleagues synthesized a series of 2-(1H-indol-3-yl)-4,6-diphenylnicotinonitrile derivatives containing pyridine and evaluated their antimalarial activity against Plasmodium falciparum. Within the tested compounds 23,24,25 three specific derivatives stood out: 4-(4-fluorophenyl)-2-(1H-indol-3-yl)-6-phenylnicotinonitrile (**23**), 4-(3,4-difluorocyclohexa-1,5-dienyl)-2-(1H-indol-3-yl)-6-phenylnicotinonitrile (**24**) and 2-(3H-inden-1-yl)-6-phenyl-4-(3,4,5-trimethoxycyclohexa-1,5-dienyl)nicotinonitrile (**25**) (Figure20) these compounds exhibited the highest

selectivity index (S.I. ranged from 3.8 to 10), indicative of their promising antimalarial potential also docking studies provided insights into the molecular mechanisms underlying the observed antimalarial activity, further supporting the potential therapeutic relevance of these compounds in combating malaria[50].

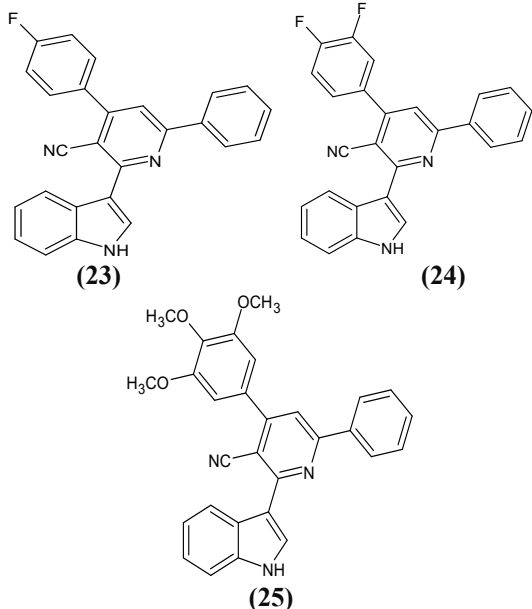


Figure:20

Luthra and colleagues identified potent antimalarial compounds, with particular emphasis on compound (Z)-methyl 2-(2-((methylamino)(phenyl)methyl)-1H-indol-3-yl)ethyl carbamate (26) (Figure21) This compound demonstrated notable activity specifically at the trophozoite stage of the parasite's growth, as reported in their study[51].

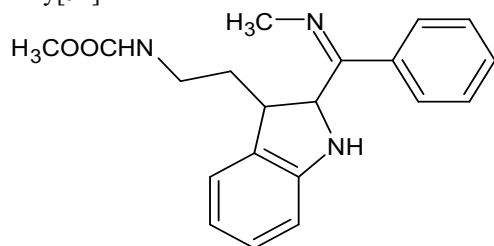


Figure:21

Yadav et al. in 2016 conducted a study involving the design and investigation of various indole derivatives for their antimalarial activity against *P. falciparum*. Notably, compound (27) (Figure22) exhibited heightened potency, with a minimum inhibitory concentration (MIC) of 0.70 µg/ml. This surpassed the efficacy of the reference drugs quinine (MIC of 0.270 µg/ml) and chloroquine (MIC of 0.02 µg/ml) [52].

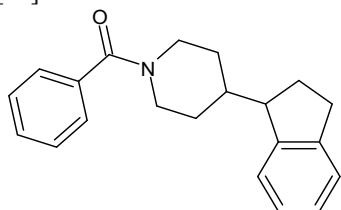


Figure:22

Schuck and colleagues, in 2014, detailed the creation of a novel set of melatonin analogs which underwent evaluation against a bacterial strain, *falciparum* culture. Among them, derivative compound (28) an analog of melatonin, demonstrated activity against *P. falciparum*, inhibiting its development [53]. The structures of the antimalarial active compounds based on indole derivatives are illustrated in (Figure 23).

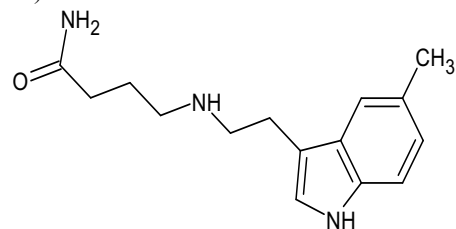


Figure:23

2.6 Antitubercular activity:

Guo et al. designed and evaluated a series of 6-cyano-5-methoxyindolo[2,3-a] carbazole derivatives with the aim of combating tuberculosis and anthrax infections. These compounds were screened for their moderate inhibitory activities against the H37Rv strain of *Mycobacterium tuberculosis* and the ANR strain of *Bacillus anthracis*. Notably, compounds such as 6-methoxy-11,12-dihydroindolo[2,3-a]carbazole-5-carbonitrile (29), 11,12-dihydroindolo[2,3-a]carbazole-5-carbonitrile (30), and 11-benzyl-11,12-dihydroindolo[2,3-a]carbazole-5-carbonitrile demonstrated moderate activity against *Mycobacterium tuberculosis*.(31)[54].(Figure 24)

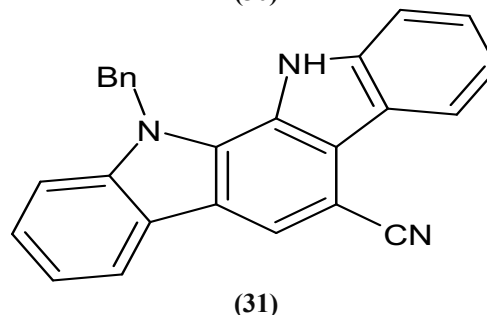
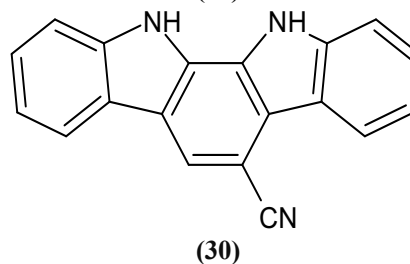
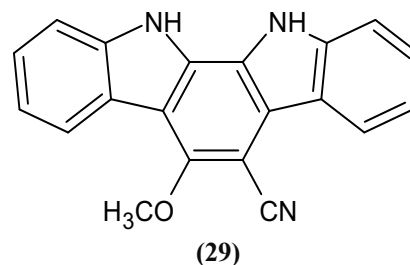


Figure:24

Ramesh et al. synthesized a library of indole chalcones and conducted screening for their antimycobacterial activity against the H37Rv strain of *Mycobacterium tuberculosis*. Among the compounds evaluated, (E)-1-(furan-3-yl)-3-(1H-indol-3-yl)prop-2-en-1-one (**32**) with a minimum inhibitory concentration (MIC) of 210 μM , (E)-3-(1H-indol-3-yl)-1-(thiophen-2-yl)prop-2-en-1-one (**33**) with an MIC of 197 μM , and (E)-2-((1H-indol-2-yl)methylene)cyclopentan-1-one (**34**) (Figure 25) with an MIC of 236 μM exhibited significant potency as drugs against *Mycobacterium tuberculosis*[55]

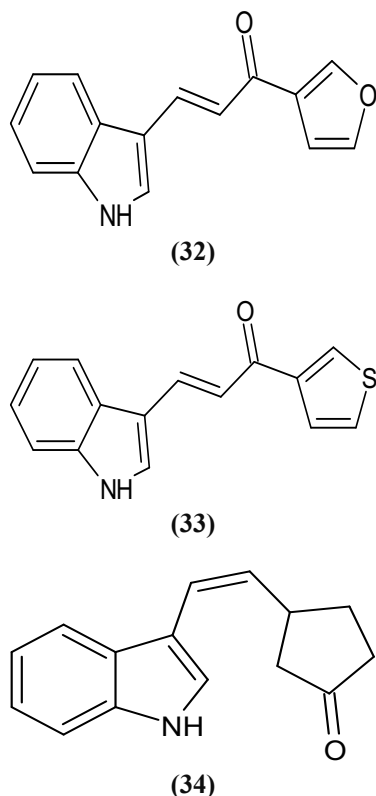
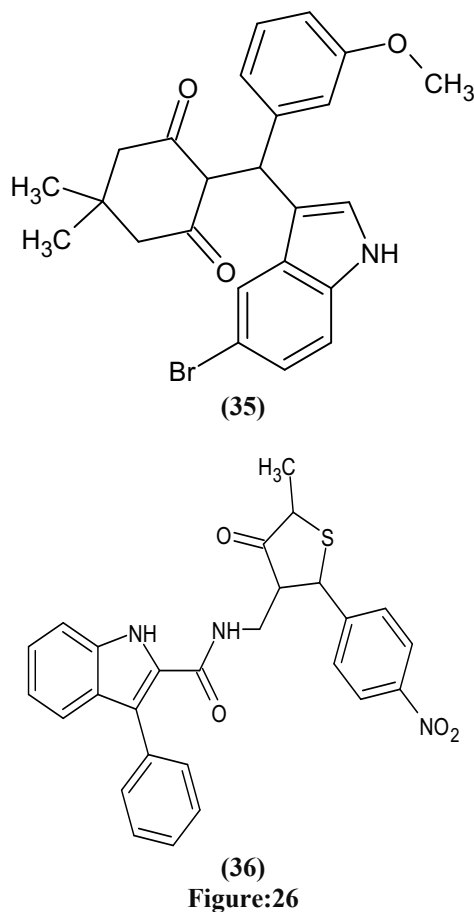
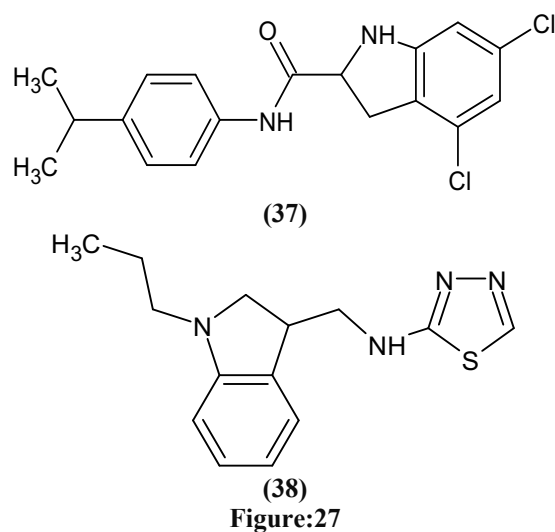


Figure:25

Khan et al. synthesized novel 3-alkylated indole derivatives using CuO as a heterogeneous catalyst in 2016. Among them, compound (**35**), with an MIC of 15 $\mu\text{g/ml}$, displayed remarkable antitubercular activity against the bacterial strain (MTCC 300) when compared to the reference drug isoniazid (MIC = 10 $\mu\text{g/ml}$)[56]. In 2016, Ustundag and colleagues prepared and investigated indole-based hydrazide-hydrazone and 4-thiazolidinones against the tubercular strain (H37 Rv). Compound (**36**), with a minimum inhibitory concentration ranging from 6.25 to 25 $\mu\text{g/ml}$, exhibited remarkable antitubercular activity compared to the reference drug rifampicin (minimum inhibitory concentration of 25 $\mu\text{g/ml}$) [57]. Shown in (Figure 26)



Tehrani et al. synthesized numerous Schiff base indole derivatives in 2014 and assessed their activity using a microtiter plate against both Gram-positive and Gram-negative bacterial strains. Compound (**37,38**) (Figure 27) with an MIC of 3.91 $\mu\text{g/ml}$, displayed higher potency compared to the reference drug ethambutol (MIC of 0.75 $\mu\text{g/ml}$) [58].



2.7 Antioxidant Activity:

Scribner and colleagues conducted research on derivatives of 2,3-diarylindoles, with amine substitutions at the 5 and 6 positions of the indole structure. In their study, various compounds were synthesized and evaluated for their potential as anticoccidial agents. Among the tested compounds, Compound (39), (Figure28) specifically 2-(4-fluorophenyl)-6-(piperidin-4-yl)-3-(pyridin-3-yl)-1H-indole, exhibited the most promising anticoccidial activity according to their findings [59].

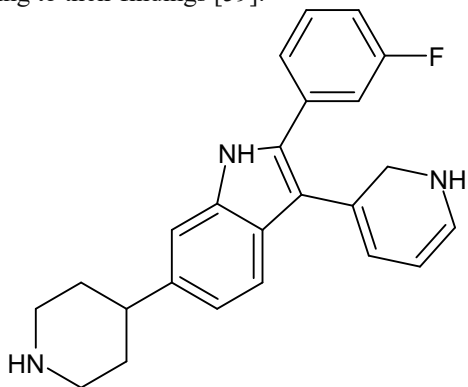


Figure:28

Yilmaz et al. synthesized and assessed the antioxidant potential of derivatives derived from 5-Chloroindole hydrazide/hydrazone. Through 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity testing, all the compounds exhibited significant antioxidant effects with IC₅₀ values ranging from 2 to 60 μM. Particularly, compound (40)(Figure29) (E)-1-((5-chloro-1H-indol-2-yl)methylene)-2-(2-chlorophenyl) hydrazine demonstrated noteworthy inhibitory activity (LP) against melatonin at a concentration of 0.1 mM, as reported in their study[60].

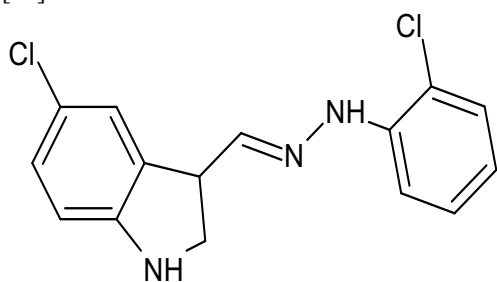


Figure:29

Orhan et al. conducted research in 2016 involving the synthesis of melatonin analogs featuring an indole moiety. The study aimed to assess the antioxidant properties and protective effects of these analogs against damage induced by β-amyloid. Compound (41a) exhibited an IC₅₀ value of 38.3 ± 8.9 μM, while compound (41b)(Figure30) showed an IC₅₀ value of 37.0 ± 2.0 μM when screened against ROS-induced oxidation. Notably, these compounds demonstrated significant efficacy comparable to the standard drug melatonin⁶¹.

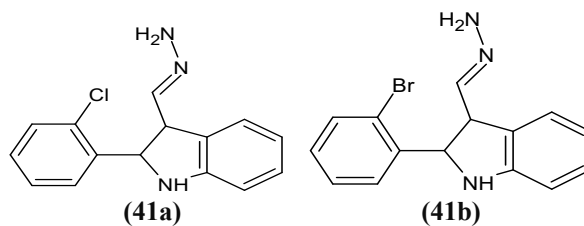


Figure:30

In a separate study by Silveira et al. in 2013, C-3 sulfonyl indoles were investigated for their antioxidant activity. Compound (42) (Figure31) with an activity level below 96.8%, exhibited higher potency in their evaluation [62].

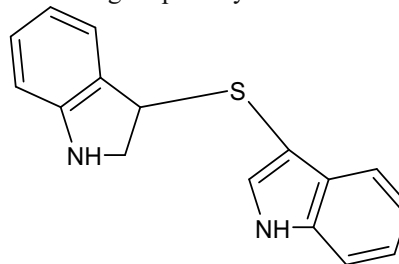
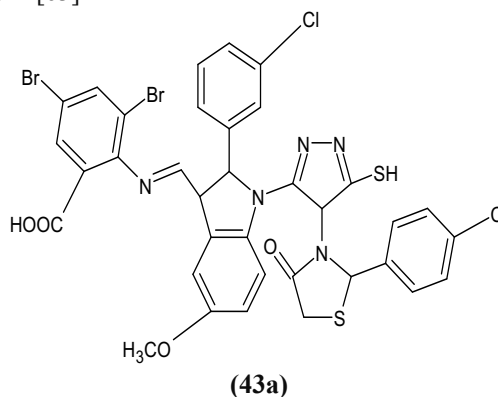


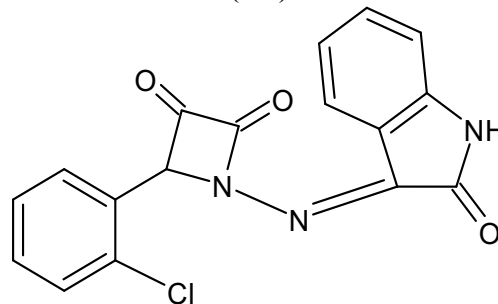
Figure:31

2.8 Antidepressant Activity:

In 2018, Kerazare et al. synthesized and evaluated oxindole derivatives containing an azetidinone moiety. The study extended to animal experimentation using a forced swim test. Compound (43 a) demonstrated a notable reduction in immobility to 66.82%, while compound (43 b) exhibited a reduction to 65.61%. These compounds, depicted in (Figure 32), displayed higher potency compared to the reference drug fluoxetine, which reduced immobility to 70.93% [63]



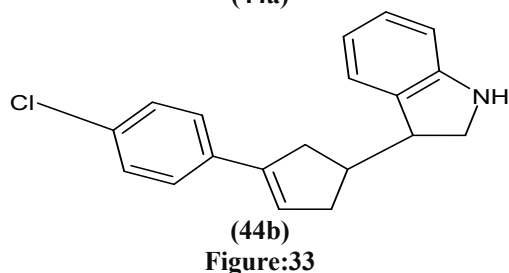
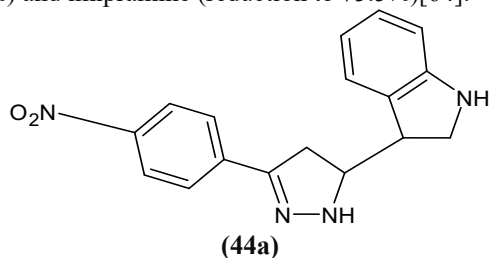
(43a)



(43b)

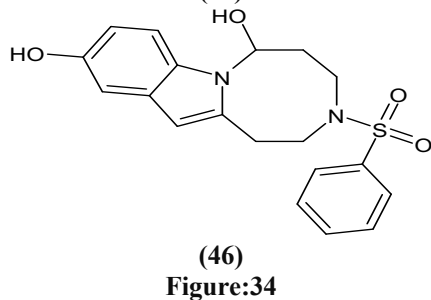
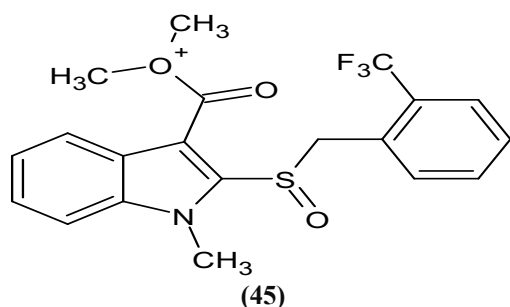
Figure:32

Additionally, Patil and Bari conducted a study in 2013, synthesizing numerous indole derivatives featuring a dihydropyrazole moiety and investigating their antidepressant activity through a forced swim test. Compound **(44 a)** displayed a reduction in immobility to 116.3 ± 1.54 , and compound **(44 b)** (Figure33) exhibited a reduction to 109.8 ± 2.86 . Both these compounds, illustrated in Figure 12, demonstrated higher potency compared to the reference drugs fluoxetine (reduction to 77.4%) and imipramine (reduction to 75.5%)[64].

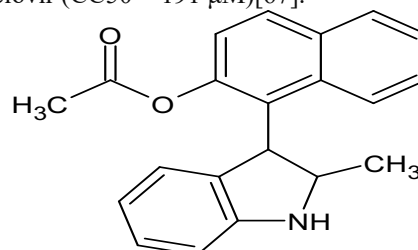


2.9 Antiviral activity:

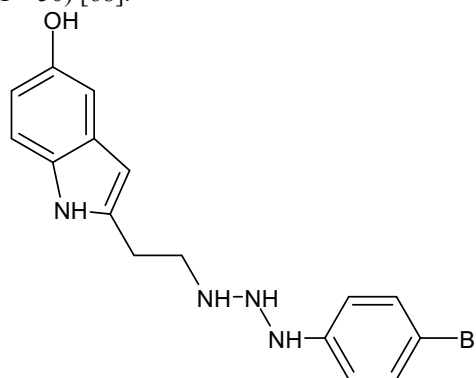
Various studies have focused on the synthesis and evaluation of indole derivatives against different viruses. In one investigation, compound **45** exhibited higher potency against the chikungunya virus ($EC_{50} = 65 \pm 1$) compared to the reference drug arbidol [65]. Chen et al. (2017) explored integrated indoles and spiroindolines against the tobacco mosaic virus. Compound **46** demonstrated elevated potency (% inhibition of $56 \pm 2\%$) compared to the reference drugs ribavirin (% inhibition of $36 \pm 1\%$) and harmine (% inhibition of $45 \pm 1\%$) at a concentration of 500 $\mu\text{g/ml}$ [66]. Shown in (Figure34).



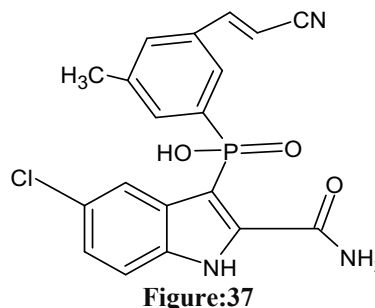
Musella et al. (2016) conducted research focused on the development and synthesis of amide-substituted indole derivatives targeting human alphaherpesvirus-3 (HHV-3). Compound **47** (Figure35) ($CC_{50} = 39 \mu\text{M}$) exhibited higher potency compared to briuvudine ($CC_{50} = 160 \mu\text{M}$) and acyclovir ($CC_{50} = 191 \mu\text{M}$)[67].



In 2009, Giampieri et al. developed indole naphthyl derivatives by fusing indole with a naphthalene nucleus. Compound **48**(Figure36) ($CC_{50} > 57 \mu\text{M}$, $SI < 5$) showed effectiveness against yellow fever virus (YFV), coxsackievirus B-2 strain (CVB-2), bovine viral diarrhoea virus (BVDV), and HIV-1, relative to reference drugs acyclovir, mycophenolic acid, and ribavirin ($CC_{50} > 100 \mu\text{M}$, $SI < 50$) [68].



Sanna and colleagues (2018) synthesized novel-indole thiourea hybrids against HIV-1. Compound **49**(Figure37) ($EC_{50} = 8.7 \pm 0.4 \mu\text{M}$) demonstrated higher potency than the standard drug efavirenz ($EC_{50} = 0.002 \pm 0.0002 \mu\text{M}$) [69].



Dussan et al. (2016) investigated various indole derivatives against HIV activity. ($EC_{50} < 0.011 \mu\text{M}$) showed highly potent anti-HIV activity [70]. Ravichandran et al. (2016) synthesized indole-7-carboxamide derivatives for anti-HIV activity, with compound **50** (Figure38) exhibiting higher potency [71].

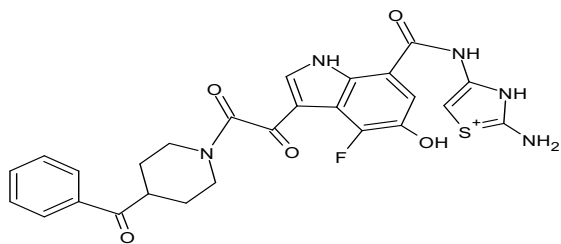
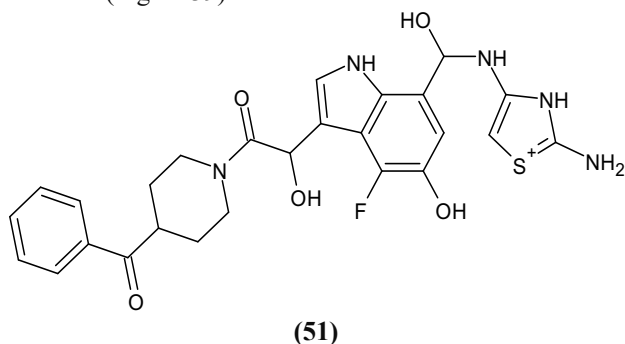
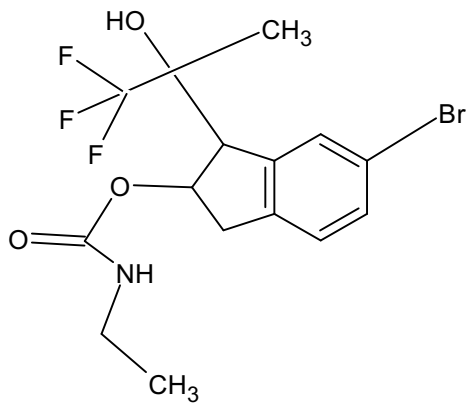


Figure:38

Ashok and colleagues (2015) synthesized indole-pyrido derivatives, with compound **51** (EC₅₀ = 0.53 μM) showing higher potency than the reference drug zidovudine (EC₅₀ = 0.002 μM)[72]. Jiang and colleagues (2014) synthesized trifluoromethyl-indole analogs with better drug resistance against anti-HIV-1 NNRTIs. Compound **51** (EC₅₀ < 133.33 μM) demonstrated higher potency than nevirapine (EC₅₀ = 0.4 μM) and efavirenz (EC₅₀ = 0.08 μM). Ferro et al. (2014) developed and investigated indole derivatives for HIV-1 integrase through a docking study. Compound **52** (IC₅₀ = 0.4 mM) exhibited maximum potency [73]. Shown in(Figure 39).



(51)



(52)

Figure:39

3. FUTURE PROSPECTS OF INDOLE DERIVATIVES DRUGS IN THERAPEUTICS:

Clinical trials are crucial in the diagnosis, treatment, and prevention of diseases. A substantial volume of data is awaiting FDA approval for the clinical trial of drugs containing indole. Indole has emerged as a promising biologically active molecule owing to its reactivity, which can be manipulated to yield various lead molecules for treating diverse ailments. Consequently, indole derivatives present potential candidates for clinical trial studies. Many

of these drugs have progressed through different phases of clinical trials and demonstrated high efficacy. However, a few compounds have shown significant adverse effects and have not been further investigated. Various indole derivatives are currently undergoing examination, with structural modifications being made to facilitate clinical trials.

CONCLUSION

This comprehensive review underscores the multifaceted biological activities of indole and its derivatives, positioning them as promising candidates for the development of novel therapeutics across various medical domains. The elucidation of the molecular mechanisms and the ongoing efforts to optimize their pharmacological profiles contribute to the growing significance of indole derivatives in the realm of drug discovery and development.

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