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Review Article

A Comprehensive Review on Biological Activities of Indolo Quinoxalines and Related Scaffold

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ABSTRACT

Indolo-quinoxaline derivatives and its related scaffold have diverse biological activity due to their structural advantages. These compounds belong to the class of polycyclic hetro-aromatic system, mainly indolo-quinoxaline are formed by the combination of two privileged heterocyclics such as, indole and quinoxaline. This review mainly focusses on the wide therapeutic activity of such compounds and effect of structural variation up on this therapeutic activity. The following section discus about the biological activities such as anticancer activity through DNA intercalation, stabilizing G-quadruplex etc., and also implies on overcoming multi drug resistance by varying the substitutions at different positions in those scaffolds and by introducing hybrid structures. These also look into the potential role of indolo-quinoxalines and related scaffolds as tool for neuroprotection by modulating pathways involved in neurodegenerative disorders and neural injuries, achieved by different means. With a focus on to the antiviral and antibacterial potential of structural diverse derivatives examined, the structurally imparted various mechanisms are revealed here. This manuscript also briefly discusses about some miscellaneous activities like antidiabetics, antifungal, antimalarial, antitubercular, antioxidant, antihistaminic and anti-inflammatory. And finally, a concise structural activity relationship also described on the basis of discussed compounds which explains the impact of different structural changes like planarity, substitutions etc., on biological activity. This section made a conclusion on the research gap of current studies.

INTRODUCTION

Indolo-quinoxaline derivatives and other condensed heterocycles have been recognized as highly important in medicinal chemistry because of their diverse biological

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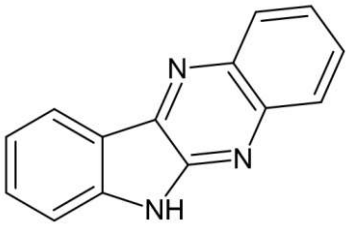
activities. The combination of electron-rich indole moieties with electron-withdrawing quinoxaline rings can mimic the natural compounds such as ellipticine and neocryptolepine. Because of their structural versatility, they can be considered as scaffolds for the design of drugs for various diseases.[1,2]

Within the field of oncology, the above-mentioned scaffolds exhibit antiproliferative activity by interacting with the DNA double helix, stabilizing G-quadruplex motifs, thereby repressing oncogene transcription, and by showing dual action against tubulin polymerization and topoisomerase 1.

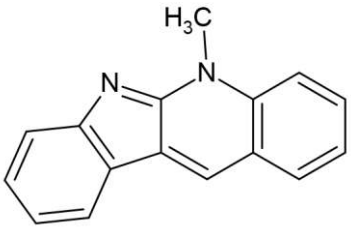
In addition to their applications in oncogenic treatment, these derivatives have been observed for their neuroprotective activity in several ways. They inhibit the activity of ionotropic glutamate receptors to defend against excitotoxicity and JNK pathways during cerebral ischemia and block amyloid β fibrillation and activate the NRF2 antioxidative pathway in conditions such as Alzheimer's and Parkinson's diseases, respectively.[3,4]

The use of Indolo-quinoxalines in drug treatment is wide-ranging, including their application as antivirals and antibiotics. Their antiviral activity arises from their capacity to stabilize the viral genome, and antibacterial activity arises from suppression of RNA synthesis controlled by genetic material. This selectivity to particular viral and bacterial actions has made them instrumental in addressing many issues currently facing.[5,6]

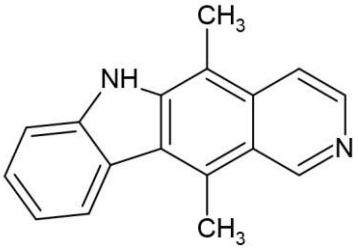
These heterocycles have been widely investigated to apply their potential in medicine for various biological activities, such as glucose metabolism regulation in type 2 diabetes cohorts, as well as affinity with several receptors, including AMPK and PTP1B. Besides, these heterocycles are known for their activity against fungi and malaria, including the mentioned strains that are resistant to conventional therapy. Moreover, their wide spectrum of pharmacological actions can be further complemented by the detection of antioxidant, antihistaminic, and anti-inflammatory actions. Therefore, this review was conducted to investigate the biological activities of indoloquinoxaline heterocycles.[7,8]



Indolo[2,3-b]Quinoxaline (IQ)



Ellipticine



Neocryptolepine

Fig 1: Core scaffold structures

Table 1: Properties of indolo-quinoxaline

Properties	Value
Molecular formula	$C_{14}H_9N_3$
Molecular weight	219.24 g/mol
Hydrogen bond donor count	1
Hydrogen bond acceptor count	2
Heavy atom count	17
Rotatable bond count	0

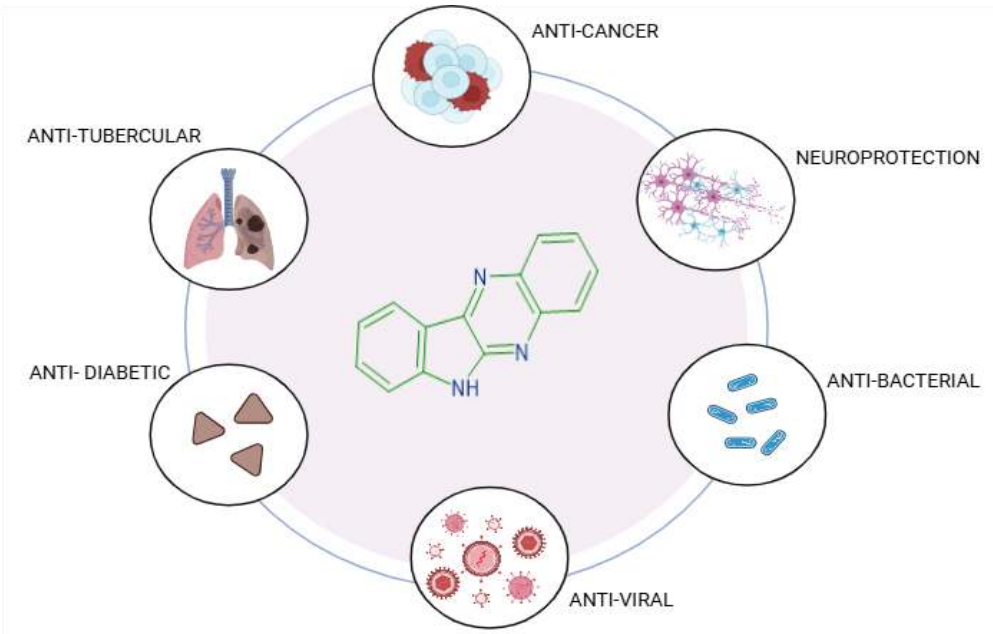


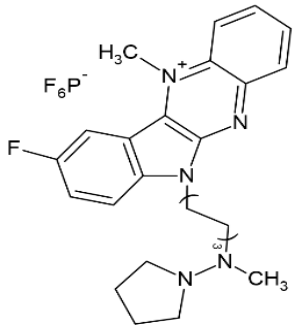
Fig 2: Illustration of activities of IQ

ANTI-CANCER

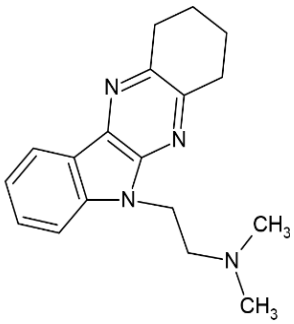
Indolo-quinoxaline and related condensed heterocyclic systems represent a privileged chemical scaffold in medicinal chemistry owing to their diverse biological activities, acting primarily as strong DNA-intercalating agents and enzyme-selective inhibitors.[9] [1] [10] [11] The combination of electron-rich indoles and electron-withdrawing quinoxalines allows these systems to be regarded as mimics of antitumor natural alkaloids such as ellipticine and neocryptolepine.[1] [2] [12]

DNA Binding and Intercalative Mechanisms

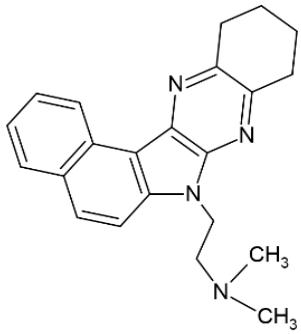
The majority of indoloquinoxaline analogs exert their cytotoxicity by intercalating the double helix of DNA, thereby interfering with cellular processes such as replication and transcription.[13] [14] [15] [11] Introducing fluorine substitution at position 9 and developing quaternary dicationic salt, compound 1 (IC_{50} = 01.80 ± 0.24 µM [MCF-7] and 4.22 ± 0.63 µM [HeLa]) prepared by Gu et al. increases the DNA binding and anticancer activity on MCF-7 and HeLa cell lines.[16] Moreover, according to a similarity search, the potential of some related isatin as minor groove binders is predicted.[17] Planarity is a key feature, as the non-planar 1,2,3,4-tetrahydro analog of compound 2 (IC_{50} = 3.75 ± 10.00 µM) decreases DNA binding ability, while extending the aromatic system through benzene annulation, as seen in compound 3-10 7H-benzoindolo[2,3-b]quinoxalines (Ig K_a = 6.23-6.87), increases binding strength.[18] [19]



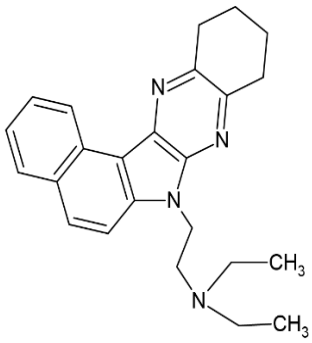
Compound 1



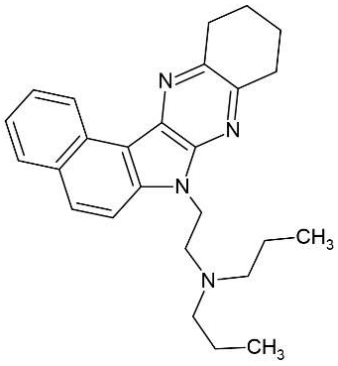
Compound 2



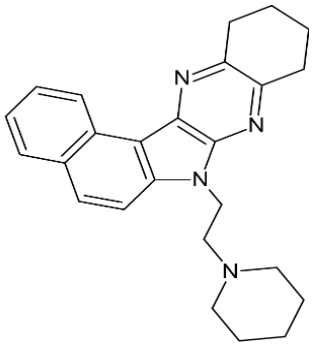
Compound3



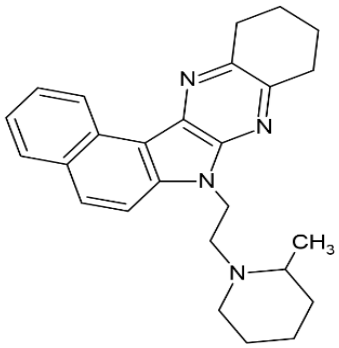
Compound 4



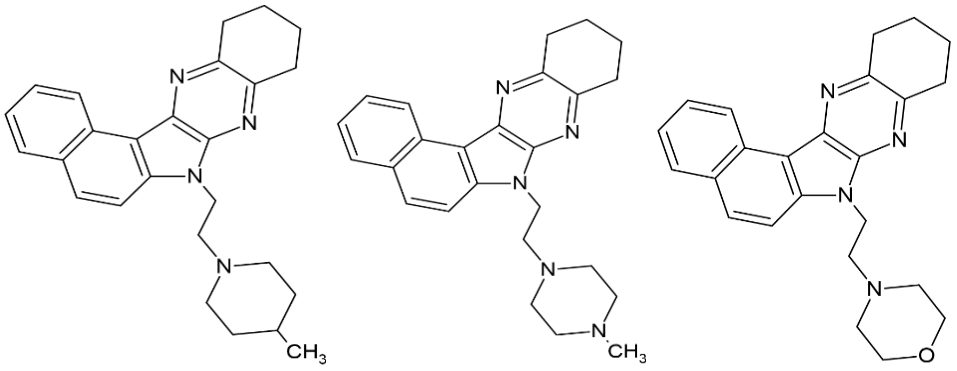
Compound 5



Compound 6



Compound 7

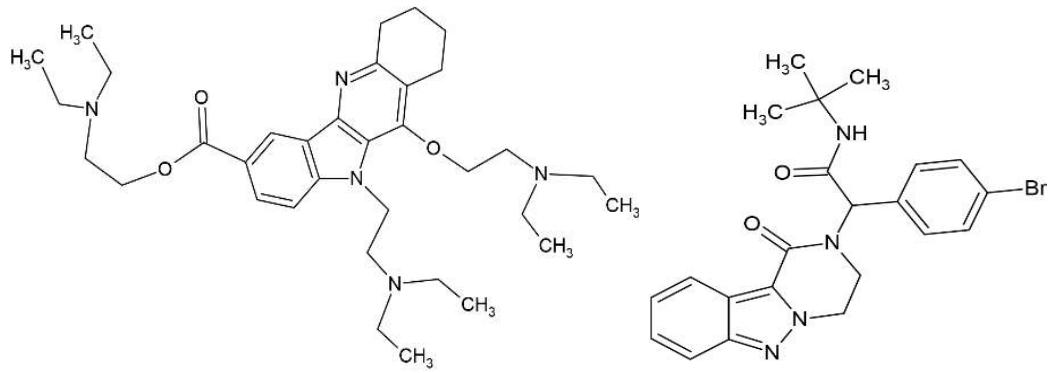


Compound 8 **Compound 9** **Compound 10**

Fig 3: Compounds with DNA binding and intercalative mechanisms

Genomic Regulation and G-Quadruplex Stabilization

The use of IQ3A compounds bearing a carboxylic acid group in position 7 and a trialkylamine moiety (compound 11; IC50 = 1.88 ± 0.10 μM), as described by Brito et al., is an effective means of stabilizing G-quadruplex (G4) in the promoter region of KRAS.[3] The effect results in the down-regulation of oncogenes and the induction of apoptosis in KRAS-dependent colon carcinoma cell lines, including HCT116 cells.[3] [2] Additionally, compound 12 (IC50 2.1 μM) by Li et al., indazolo-fused quinoxalinones synthesized through Ugi/Ullmann cascades, has shown high antiproliferative potency against HCT116 cells.[20]



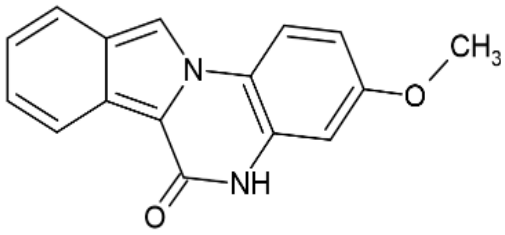
Compound 11 **Compound 12**

Fig 4: compounds show genomic regulation and G-quadruplex stabilization

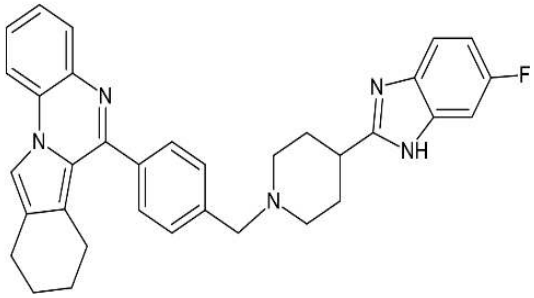
Dual Inhibition, Cell Cycle Arrest, and AMPK Apoptosis

Some isoindolo[2,1-a]quinoxaline derivatives, namely compound 13 (IC_{50} = 0.02 ± 0.002 μM) (Diana et al.), constitute an innovative class of molecules endowed with

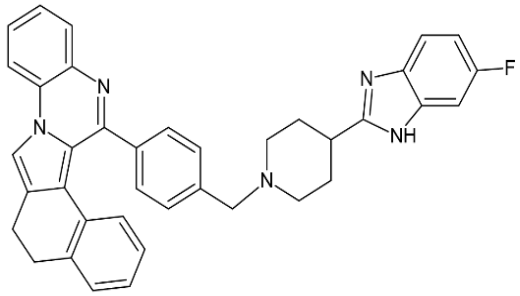
inhibitory activity on tubulin polymerization and topoisomerase I. Such a molecule resulted in blocking at the G_2/M phase and mitochondria depolarization in sixty human cancer cell lines.[21] Likewise, compounds 14-16 (IC_{50} = 3.5 ± 0.3 µM, 4 ± 0.3 µM, 4 ± 0.3 µM) (Desplat et al.) isoindolo and indolo bioisosteres bearing benzyl piperidinyl fluoro-benzimidazoles proved to be effective against different leukemic cell lines.[22] Neocryptolepine analogue compounds 17-20, Altwaijry et al., further reveal their antitumor potential by increasing cell aggregation in G_0/G_1, S, and G_2/M phases, leading to clear apoptotic populations.[23]



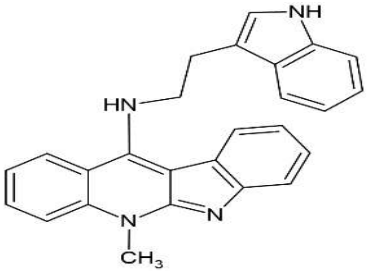
Compound 13



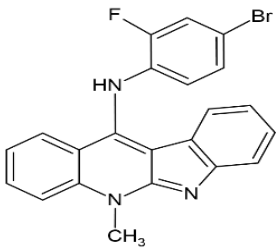
Compound 14



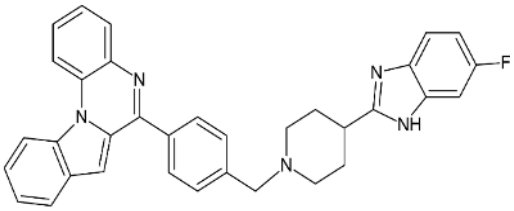
Compound 15



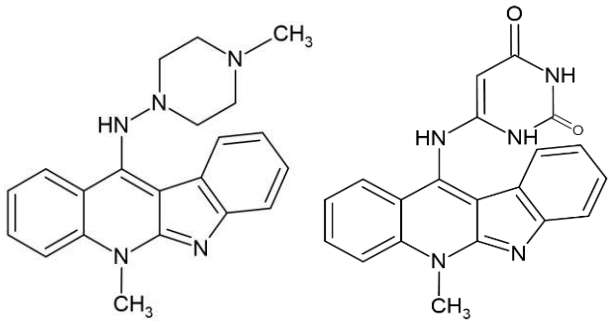
Compound 16



Compound 17



Compound 18

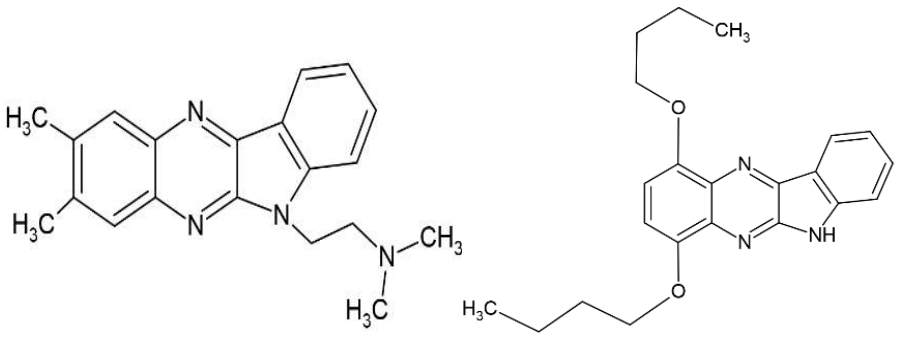


Compound 19 **Compound 20**

Fig 5: compound exhibits dual inhibition, cell cycle arrest, and AMPK apoptosis

Overcoming Resistance and Chemoprevention

Through strategic substitutions, the ability for these scaffolds to overcome multi-drug resistance was achieved; for example, Compound 21 (IC_{50} > 50 µg/mL), which selectively inhibits P-glycoprotein (Pgp) and renders drug-resistant tumor cells sensitive to conventional chemotherapy agents, such as doxorubicin.[24] Regarding to chemoprevention, Compound 22 by Skarin et al. demonstrated substantial protective activity against skin tumor promotion in mice.[25] [26].



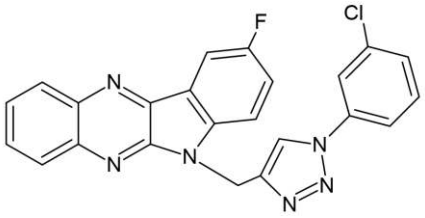
Compound 21 **Compound 22**

Fig 6: compound overcoming resistance and chemoprevention

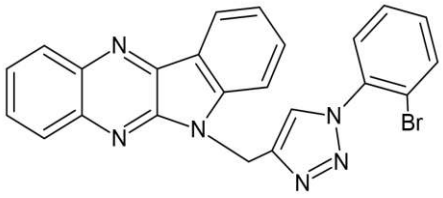
Broad-Spectrum Activity and Hybrid Scaffolds

Screenings of various series have yielded highly potent 6-aralkyl-9-substituted derivatives against human leukemia and reproductive organ cancer cell lines.[27] [13] [28] [29] Compounds 23-25 by Avula et al. demonstrated selective activity against reproductive pathways. In this group, compounds 23 and 24 (cell viability = 72.64±4.97 and 73.17±2.82) exhibited a 30% cytotoxic activity against the DU-145 prostate cell line, whereas compound 25 (cell viability = 75.59±3.14) appeared to be more potent against the HeLa cell line, assessed with other derivatives.[27] [28] Potentiality of the derivatives is further enhanced by

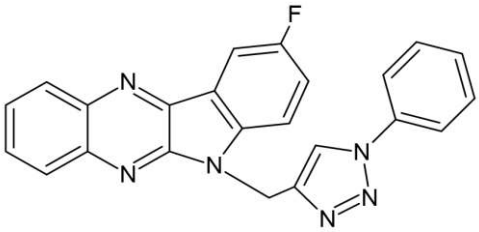
conjugating them with other drugs like artesunate or preparation of N-glycosides.[30] [29] Recently, novel derivatives such as 26, reported by Samorodova et al., 26 spectral investigations are currently underway with dyes based on the indoloquinoxaline structure and palladium-catalyzed green synthesis method.[31] [32]



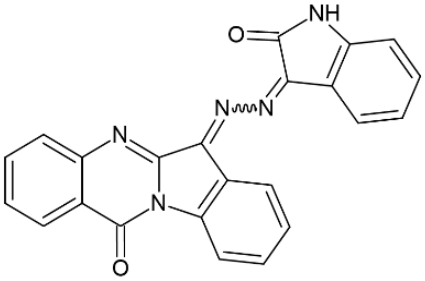
Compound 23



Compound 24



Compound 25



Compound 26

Fig 7: compound with broad-spectrum activity and hybrid scaffolds

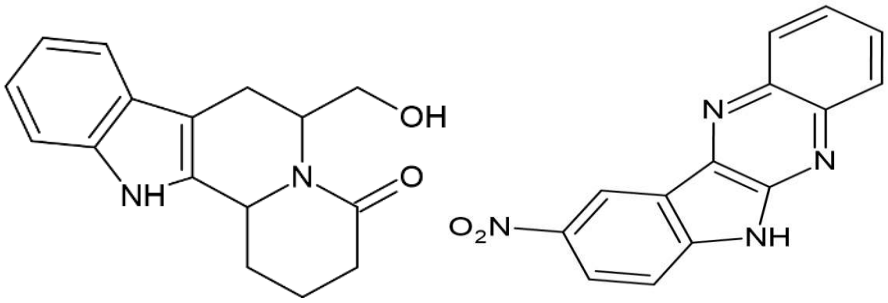
NEUROPROTECTION

The indoloquinoxaline framework, along with its derivatives, has been shown to be a versatile tool for neuroprotection by modulating pathways involved in neurodegenerative disorders and neural injuries.[33] [34] This is achieved by means of the manipulation of glutamate receptors, the inhibition of kinases such as JNK, and the induction of antioxidants like NRF2.[4] [34]

Modulation of Ionotropic Glutamate Receptors

Neuronal death caused by excitotoxicity due to hyperstimulation of glutamate receptors on neurons is a major factor responsible for ischemia and neurodegeneration.[35] Compound 27 by Nuno A. L. Pereira et al., (30.4±2.5) (Indolo-[2,3-a] quinolizidines) has been developed as a highly potent modulator of the N-methyl-D-aspartate (NMDA) receptor, providing protection against NMDAR-induced neuronal death.[36] Additionally, via in silico screening studies, compound 28 (DSX Binding Score = -107.35), Balasundaram et al., has been recognized as an allosteric

inhibitor of the iGluA2 (AMPA) receptor, which could serve well.[35]

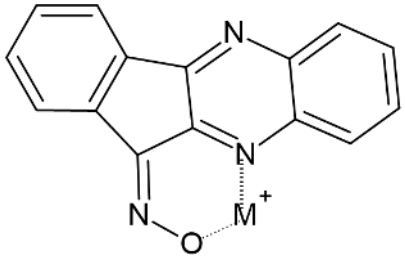


Compound 27 **Compound 28**

Fig 8: compounds exhibit modulation of ionotropic glutamate receptors

Inhibition of c-Jun N-terminal Kinases (JNK) in Cerebral Ischemia

Neuronal damage caused by reperfusion-mediated oxidative stress is significantly influenced by the JNK signalling pathway. The lithium salt of 11H-indeno[1,2-b]quinoxaline-11-one oxime, or IQ-1L (compound 29- Kd = 0.14 ± 0.01 μM[JNK], 5.80 ± 0.70 [NRF2]), is a powerful JNK inhibitor. IQ-1L reduced the infarct area by 52% in relative to vehicle control and significantly improved neurological score assessments in rat models of focal cerebral ischemia.[34]



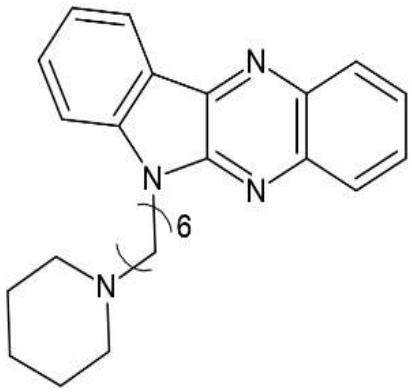
Compound 29

Fig 9: compound Inhibit JNK in Cerebral Ischemia

Multifunctional Anti-Alzheimer Activity

MTDLs for Alzheimer's disease are being investigated as derivatives of indolo-quinoxalines. Compound 30 (AchE- 5.80 ± 0.70, BuChE- 0.96 ± 0.31) Kanhed et al., have the ability to function as both amyloid beta (Aβ1-42) fibrillation blockers and cholinesterase inhibitors (BuChE specifically). It is believed that the indoloquinoxaline framework's flat, planar

arrangement prevents pi-pi stacking in amyloid fibrils. [33]

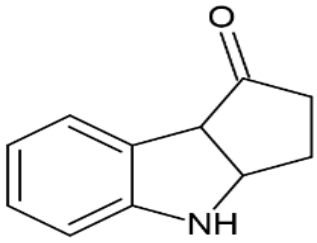


Compound 30

Fig 10: compound with multifunctional anti-alzheimer activity

Regulation of the NRF2 Pathway in Parkinson's Disease

Indole-derivative-related scaffolds, such as compound 31 (NC001-8), have been shown to provide neuroprotection against dopaminergic neuronal loss in Parkinson's disease. By increasing the NRF2 antioxidative pathway, which lowers ROS levels and prevents apoptosis, NC001-8 enhances neuronal survival. To activate downstream antioxidant genes such as NQO1, this regulation entails the translocation of NRF2 into the nucleus.[4]



Compound 31

Fig11: compound regulate NRF2 pathway in Parkinson's disease

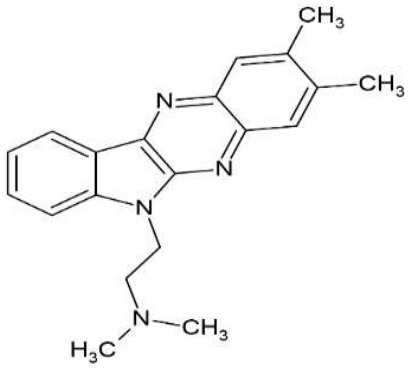
ANTI-VIRAL ACTIVITY

As aza-analogues of the cytotoxic alkaloids cryptolepine and ellipticine, indolo[2,3-b]quinoxalines' pharmacological profiles have shifted toward highly specific antiviral drugs by structural optimization.[9] [14] DNA intercalation, which is defined by the planar aromatic core inserting between nucleic acid nucleobases, is the main mode of

action for these heterocycles.[37] [11] This interaction stabilizes DNA triple helices and interferes with critical steps of viral replication, particularly the uncoating of the viral genome.[25] [37] Moreover, aminoethyl substituted derivatives are potent endogenous interferon (IFN) inducers, thus boosting the host's innate immunological defense against DNA and RNA viruses.[5] [6]

Disruption of Viral Uncoating via DNA Intercalation

Compound 32 (B-220) (Wilhelmsson et al., 2008) is used as a traditional DNA intercalator, exhibiting remarkable antiviral activity against the herpes viruses, namely human cytomegalovirus (HCMV), HSV-1, and VZV.[1] [25] [37] [11] From spectroscopic studies, it is found that these compounds display a specific affinity for AT-region genome sequences, which are important in targeting the viral genome at the time of de-capsulation.[37] Moreover, the thermal stability of these frameworks, often used in optoelectronic dyes, increases their rigidity during intercalation and enhances their effectiveness in stabilizing the viral genome during the decapsulation pathway.[31] [32]

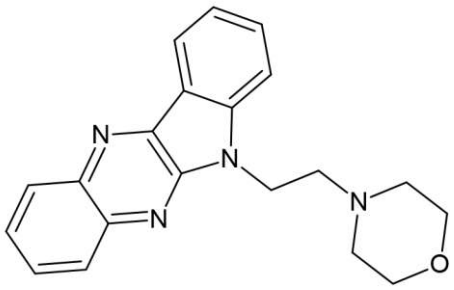


Compound 32

Fig 12: compound disrupt of viral uncoating via DNA intercalation

Induction of Endogenous Interferon (IFN)

The specific aminoethyl analogs, including Compound 33 for VSV, exhibit strong interferon (IFN)-inducing activity.[5] [38] [6] Such analogues show higher antiviral activity when used in a prophylactic mode (24 hours prior to infection) rather than a therapeutic one, which is a hallmark of a cytokine-based mechanism of protection.[38] [18] The studies conducted on Compound 33 reveal its high efficiency in inducing a long-lasting IFN response without a significant increase in inflammatory markers (MCP-1, complement).[6]

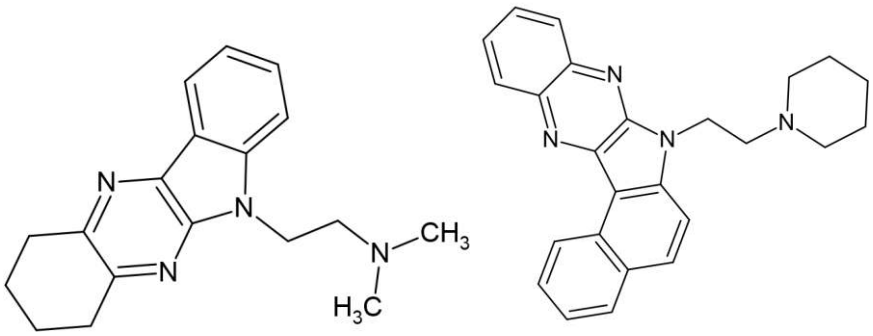


Compound 33

Fig 13: compound show induction of endogenous interferon

SAR: Influence of Molecular Planarity and Annulation

SAR investigations have demonstrated that molecular planarity is mandatory for achieving high DNA-binding efficiency and antiviral efficacy.[19] For instance, non-planar derivatives like tetrahydro-indolo quinoxaline (Compound 34) exhibit less intercalation potential than their fully aromatic counterparts. On the other hand, while adding an additional benzene ring to maximize the compound's protection (Compound 35) improves its DNA-binding ability, this modification may lead to decreased direct antiviral and IFN-inducing properties, suggesting that the tetracyclic structure is more suitable for antiviral applications.[19] [18]



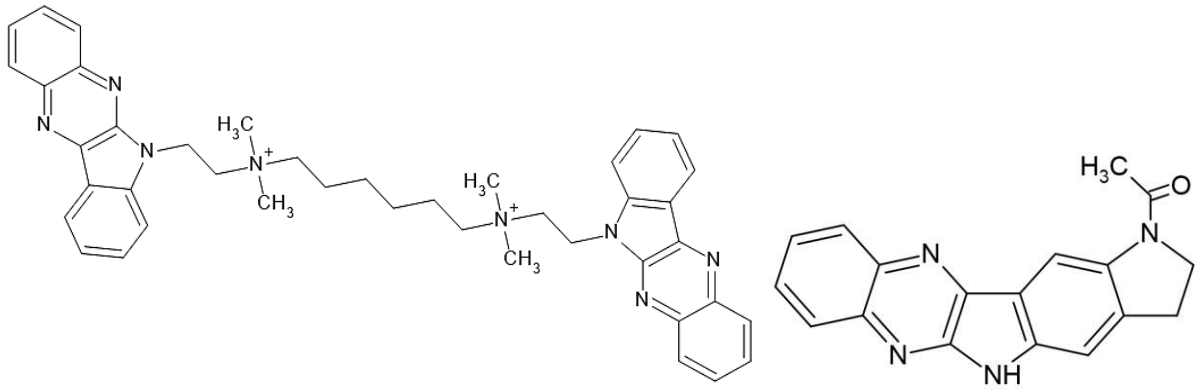
Compound 34 **Compound 35**

Fig 14: compounds have influence in antiviral activity based on its SAR

High-Potency Dimeric and Novel Heterocyclic Scaffolds

The current advancements in organic synthesis strategies, especially the implementation of green chemistry approaches employing the catalyst, have made it possible to create highly efficient dimeric indoloquinoxaline derivatives (Compound 36).[9] [10] [37] The dissociation constants of these dimeric systems are much higher than those of the

corresponding monomers and have greater efficacy than that of conventional antiviral compounds such as ganciclovir.[37] Additionally, the creation of novel pentacyclic heterocyclic systems (Compound 37), which are claimed to provide a high yield of 71.6% (Bobokhidze, 2024) through palladium-assisted C–C and C–N couplings, has led to new perspectives on designing next-generation intercalating antiviral drugs.[1] [31]



Compound 36 **Compound 37**

Fig 15: high-potency dimeric and novel heterocyclic scaffolds

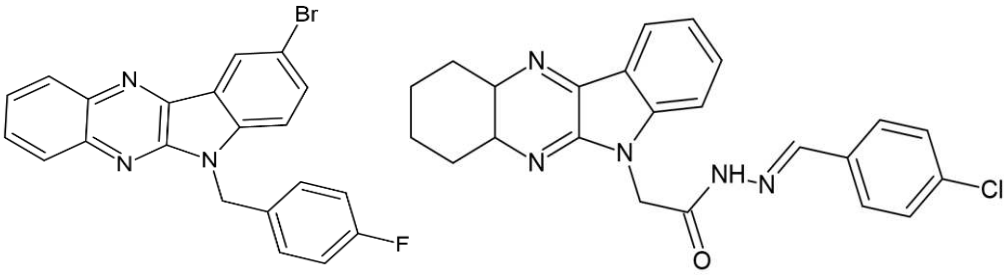
ANTI-BACTERIAL

Indolo[2,3-b]quinoxalines (IQ) and their analogs are an extremely significant group of nitrogenous heterocyclic molecules, which have been extensively utilized in medicinal chemistry to act as antibacterial agents.[32] [9] Quinoxaline derivatives have been found to show considerable medicinal significance, including antibacterial action.[2] [37] The biological significance of indolo[2,3-b]quinoxaline derivatives is well recognized, especially their antibacterial activity against both Gram-positive and Gram-negative bacteria. [31] [40] [41] [42]

Prevention of DNA-Directed RNA Synthesis

The antibacterial efficacy of all the selected compounds was examined in vitro against *MRSA, E. coli, and K. pneumoniae*, utilizing the agar cup diffusion technique for the screening of susceptibility testing and twofold serial dilution for the determination of MIC. Quinoxalines exhibit strong antimicrobial properties due to their ability to inhibit DNA-dependent RNA synthesis by interfering with the binding to CpG sites on DNA.[40] Compound 38, Abdu-Allah et al. revealed the highest activity against the three strains, even exceeding the reference drug (gentamycin) with a MIC value of 25.00 ± 00 µM/mL against E. coli.[40] The results of screening revealed that the substituted quinoxaline compounds having electron-withdrawing groups mediated moderate to significant antibacterial activity as compared

to the standard drug ciprofloxacin.[41] Gupta et al. (2013) reported Compound 39 was found to exhibit the most potent in vitro antimicrobial activity with the MIC value of 14.00 ± 00 µg/ml against *Staphylococcus pyogenes*.[41]

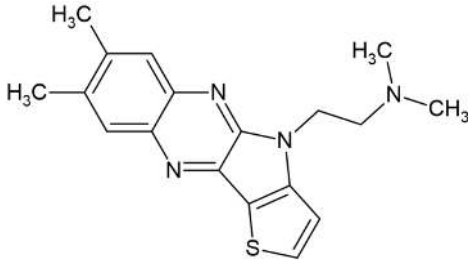


Compound 38 **Compound 39**

Fig 16: compound Inhibit JNK in Cerebral Ischemia

Inhibition of Mycobacterium Adenosine Kinase (Rv2202c)

In the first study, these polycyclic compounds were tested for their antimycobacterial activity, including against extensively drug-resistant strains, and facilitated a moderate bacteriostatic effect against Mycobacterium tuberculosis H37Rv.[7] Molecular docking data suggest that 4-alkyl-4H-thieno[2′,3′:4,5]pyrrolo[2,3-b]quinoxalines are likely inhibitors of adenosine kinase (Rv2202c).[7] Compound 40 Sadykhov et al. demonstrated a MIC value of 12.50 ± 0.00 µg/mL against both the H37Rv strain and an extensively drug-resistant (XDR) strain of Mycobacterium tuberculosis with an IC50 value of 11.80 ± 1.40 µg/mL against Vero cells.[7]



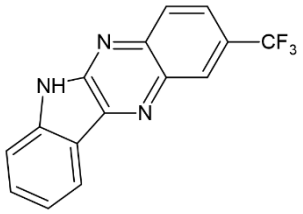
Compound 40

Fig 17: compound Inhibit Mycobacterium Adenosine Kinase

In Vitro Growth Inhibition of Pathogenic Strains

All the synthesized compounds were also screened in vitro for antibacterial assay against Gram-negative (*Escherichia coli* and *Staphylococcus aureus*) and Gram-positive (*Salmonella typhi* and *Bacillus subtilis*) pathogenic bacteria in comparison to the standard streptomycin.[39] It was observed

that the compounds bearing b electron-donating and -withdrawing groups exhibited varying degrees of potent activity against bacterial and fungal strains.[39] Compound 41 has an excellent Inhibition Zone (IZ) value of 21.00 ± 0.00 mm against S. aureus, as shown by Durgarao et al.[39]

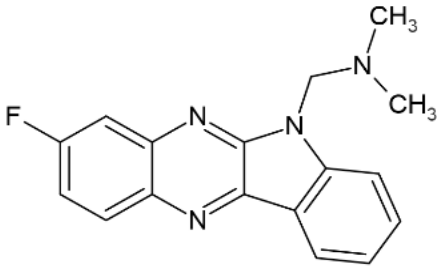


Compound 41

Fig 18: compound perform in vitro growth inhibition of pathogenic strains

MISCELLANEOUS ACTIVITY

Anti-Diabetic Activity: In medicinal chemistry, indolo[2,3-b]quinoxaline derivatives are considered crucial for several medicinal applications, including antidiabetic activity.[7] Compound 42 (Kunjiappan et al., efficiency of glucose utilization 58.56 ± 04.54% at 40 mg) was encapsulated into keratin nanoparticles for regulating glucose metabolism in 3T3-L1 adipocytes.[8] The molecules possess significant interactions within the binding sites of AMPK and PTP1B, two crucial therapeutic targets for treating type 2 diabetes based on molecular docking analysis.[8] Molecular docking studies and computational techniques were employed for evaluating other similar frameworks, such as substituted benzimidazoles, for potential anti-diabetes properties.[10]

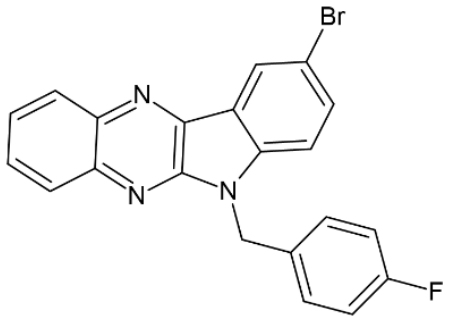


Compound 42

Fig 19: anti-diabetic compound

Anti-Fungal Activity: Fungus-borne disease infections have become quite common, which necessitated the development of newer indoloquinoxaline antimycotics.[41] Compound 39 (Gupta et al., MIC values of 28 and 19 µg/ml against *Candida albicans* and

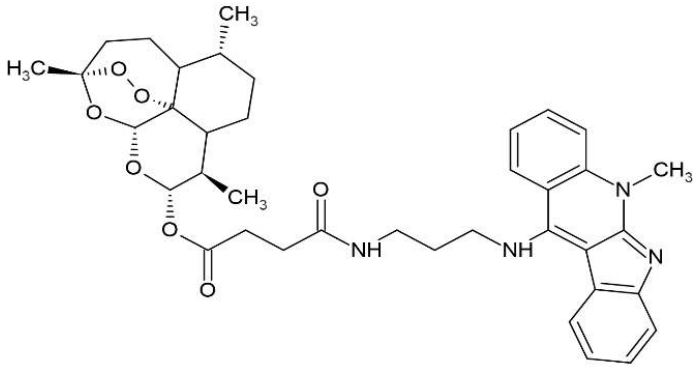
Aspergillus niger, respectively) was the most effective antifungal compound in its class.[41]



Compound 39

Fig 20: compound exhibit anti-fungal activity

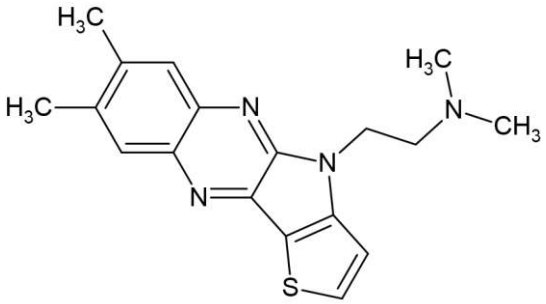
Anti-Malarial Activity: The quinoxaline and indolo-quinoline derivatives are famous for their activity against malaria.[10] Another compound, 43 (Wang et al., 02.10 ± 00.00 nM vs. NF54), was developed as an effective antimalarial agent. [29] Such hybrids affect erythrocytic forms of parasites, including those resistant to chloroquine.[29]



Compound 43

Fig 21: compound exert anti-malarial activity

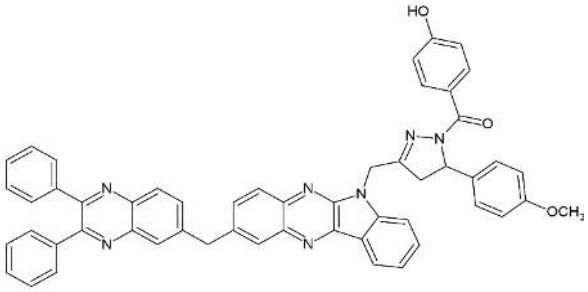
Anti-Tubercular Activity: The antimycobacterial activity of new polycyclic derivatives, including 4-alkyl-4H-thieno[2′,3′:4,5]pyrrolo[2,3-b]quinoxalines, against *Mycobacterium tuberculosis* H37Rv was tested.[7] Compound 40 (Sadykhov et al., MIC 12.50 µg/mL) correlated with antitubercular activity against susceptible and extensively drug-resistant (XDR) strains.[7] Quinoxalines are also known to have strong anti-mycobacterial properties in general drug discovery settings. [43]



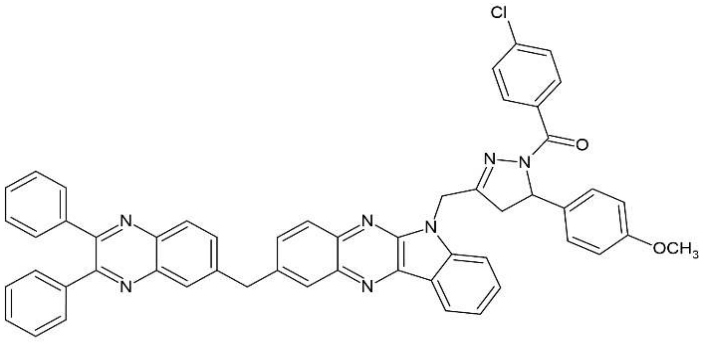
Compound 40

Fig 22: compound shows anti-tubercular activity

Antioxidant and Antihistaminic Activity: Phenylpyrazolo indoloquinoxaline derivatives: A study of their multifunctional pharmacological profile. [44] Compound 44 (Sridevi et al., 59.40%) demonstrated superior free radical scavenging activity in DPPH tests.[44] Compound 45 (Sridevi et al., protection 90.9%) demonstrated strong antihistamine effects in guinea pig tests using the histamine chamber method.[44]



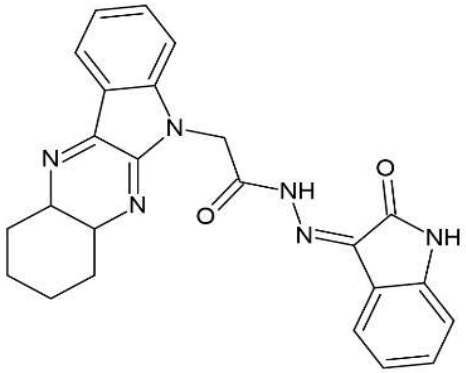
Compound 44



Compound 45

Fig 23: compounds with antioxidant and antihistaminic activity

Anti-Inflammatory Activity: Novel hexahydro indoloquinoxaline compounds were produced and tested for in vivo anti-inflammatory efficacy using carrageenan-induced rat paw edema techniques.[40] Compound 46 (Abdu-Allah et al., edema inhibition 79.00% at 5 hours) was the most active drug in the series. [40]



Compound 46

Fig 24: anti-inflammatory compound

Stuctural Activity Relationship of Indolo-Quinoxaline

Table 2: SAR Table for Indolo-quinoxaline Derivatives

Structural Feature / Modification	Biological Effect / Activity Relationship	Example Compound(s)
Molecular Planarity	Mandatory for efficient DNA intercalation and binding. Non-planar analogs exhibit significantly decreased binding ability.	Compound 2, 30, 34
Benzene Annulation	Extending the aromatic system increases DNA-binding strength, though it may decrease direct antiviral or interferon-inducing properties.	Compounds 3, 10, 35
Position 9 Substitution (Fluorine) & Quaternary Dicationic Salts	Increases DNA binding affinity and anticancer activity specifically against MCF-7 and HeLa cell lines.	Compound 1
Aminoethyl Substitutions	Act as potent endogenous interferon (IFN) inducers, enhancing the host's innate immunological defense against viruses.	Compound 33
Strategic Substitutions for Resistance	Allows the scaffold to selectively inhibit P-glycoprotein (Pgp), rendering drug-resistant tumor cells sensitive to chemotherapy.	Compound 21
Dimerization (Dimeric Systems)	Results in significantly higher dissociation constants and greater antiviral efficacy compared to corresponding monomers.	Compound 36
Electron-Withdrawing Groups on Quinoxaline	Correlates with moderate-to-significant antibacterial activity against strains like *E. coli* and MRSA.	Compound 38

4-Alkyl-4H-thieno Fusion	Shifts activity toward Mycobacterium Adenosine Kinase inhibition, providing potent antitubercular effects against XDR strains.	Compound 40

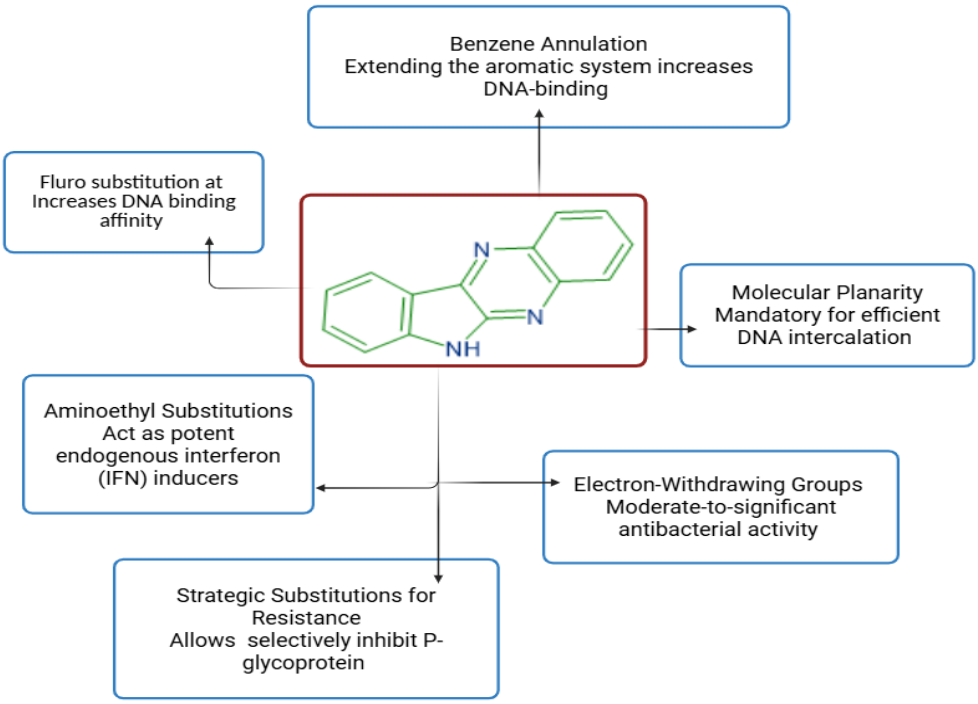


Fig 25: SAR illustration of indolo-quinoxaline

CONCLUSION

This review highlights the diverse biological activities of indolo-quinoxaline and related chemical frameworks, particularly their anticancer, neuroprotective, antiviral, antibacterial, and other effects, such as antidiabetic, antifungal, antimalarial, antitubercular, antioxidant, antihistaminic, and anti-inflammatory activities. These findings suggest that quinoxaline architectures interact with various biological targets. A comparison of structure and activity reveals that structural changes, such as annulation, fluorination, carboxylic acid substitution, and addition of electron-withdrawing groups, significantly modulate biological activity and therapeutic potential. The review also summarizes evidence supporting the biological potential of indolo-quinoxaline derivatives, established through experimental and computational methods, including MTT cytotoxicity assays, molecular docking, DNA binding, enzyme inhibition, antimicrobial and antiviral screenings etc. However, none of the existing studies examine toxicity, indicating a need for further research in this area. Additionally, many derivatives remain unexplored, suggesting more opportunities for future application. The study areas can also be improved by incorporating several in-vivo and in-vitro analysing methods. Indolo-quinoxaline-based compounds hold great

potential for successful drug development and future therapeutic applications via proper structural optimization and pharmacological evaluation.

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