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Evaluation of the Pharmacological Profiles of Quinoline-Based Compounds

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ABSTRACT

Quinoline-based compounds represent a diverse class of molecules with promising pharmacological activities across various therapeutic areas. This abstract provides a concise overview of recent advancements in the evaluation of the pharmacological profiles of quinoline-based compounds, focusing on their potential as therapeutic agents. The pharmacological evaluation of quinoline-based compounds spans several therapeutic areas, including, antiviral, anticancer, cardiovascular, anti-convulsant, anti-malarial, anthelmintic, activities.

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INTRODUCTION

QUINOLINE

Quinoline, also known as 1-aza-naphthalene, exhibits characteristics of a weak tertiary base, forming salts with acids and engaging in reactions akin to pyridine and benzene. Its versatile nature allows for both electrophilic and nucleophilic substitution reactions. Notably, it's deemed safe for human consumption through oral absorption and inhalation, showcasing a broad spectrum of medicinal properties including antimalarial, antibacterial, antifungal, anthelmintic, cardiotonic, anticonvulsant, anti-inflammatory, and analgesic effects attributed to its quinoline ring structure.[1]

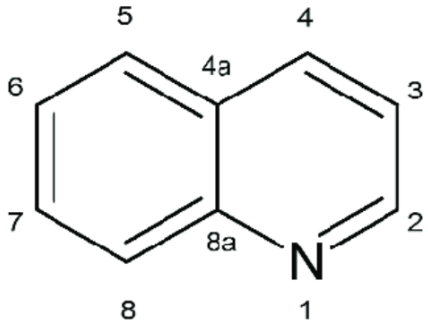

Fig no :1 Quinoline

Table no :1 Properties of quinoline.

IUPAC NAME	1-aza-napthalene
MOLECULAR FORMULA	C_9H_7N
MOLECULAR WEIGHT	129.16.
LOG P VALUE	2.04
ACIDIC pK_b	4.85
BASIC pK_a	9.5

CHEMISTRY OF QUINOLINE

Quinoline, characterized by the chemical formula C9H7N, is an aromatic heterocyclic organic compound formed by the fusion of a benzene ring with a pyridine ring. Its aromatic nature stems from the benzene ring, with this aromaticity extending to the nitrogen atom within the pyridine ring, thus enhancing quinoline's overall stability.[2]

SYNTHESIS OF QUINOLINE

Skraup-Doebner-Von Miller reaction

The Skraup and Doebner-Miller syntheses of quinolines follow analogous reaction pathways, both commencing with the interaction between aniline (C-C-N) and α,β-unsaturated carbonyl (C-C-C) compounds.[3]

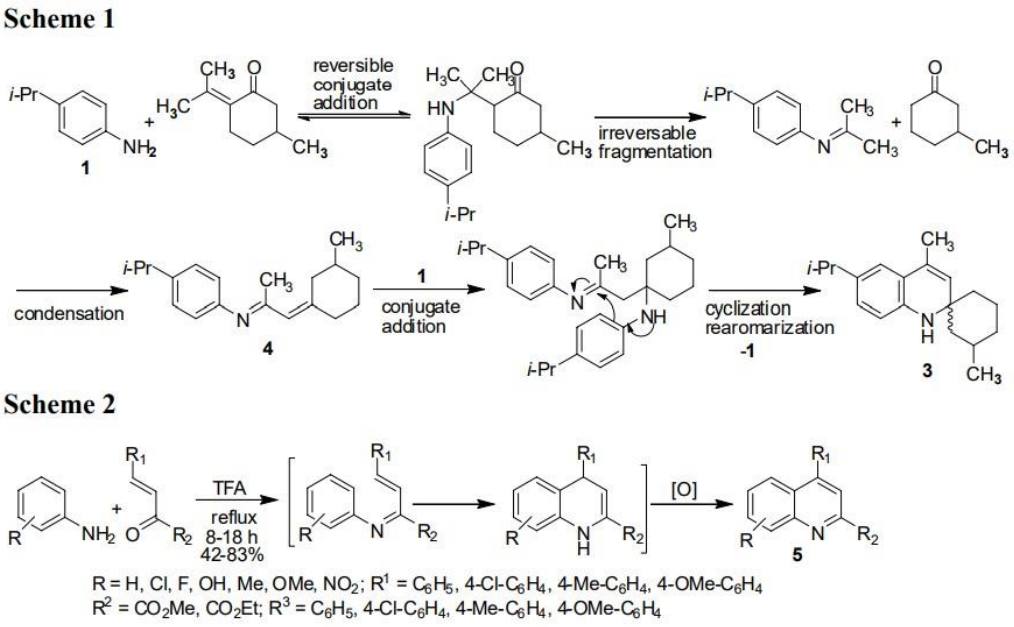

Fig no :2 Synthesis of quinoline

PHARMACOLOGICAL ACTIVITY

ANTI-CANCER ACTIVITY

Quinoline serves as a promising scaffold for the development of anticancer drugs, as its derivatives exhibit potent effects through various mechanisms such as apoptosis induction, disruption of cell migration, inhibition of angiogenesis, modulation of nuclear receptor responsiveness, and cell cycle arrest. These properties have been demonstrated in numerous cancer cell lines including breast, colon, lung, colorectal, and renal cancers. One notable quinoline derivative, dictamnine, has shown significant anticancer activity. Experimental evidence suggests that dictamnine effectively reduces migration and invasion, inhibits cell proliferation, and promotes apoptosis in HCT116 cells by downregulating key factors such as HIF-1α and Slug. In vivo studies further support dictamnine's efficacy, demonstrating

substantial inhibition of tumor growth in xenograft models. These findings underscore the potential of dictamnine as a potent inhibitor of cancer, warranting further exploration for pathway-targeted anticancer therapy.[4]

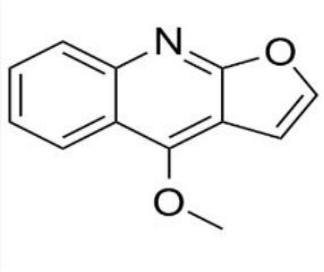

Fig no:3 Dictamine

ANTI-CONVULSANT ACTIVITY

Nithyanantham Muruganantham elucidated the anticonvulsant properties of specific quinoline derivatives. Through the synthesis and evaluation of a series of 8-substituted quinolines, their efficacy against seizures induced by maximal electro shock (MES) and pentylenetetrazole (scMet) was assessed. Notably, derivatives containing a 2-hydroxypropyloxyquinoline moiety exhibited remarkable anticonvulsant activity. Compound (8-(3-(4-phenylpiperazino)-2-hydroxypropyloxy)quinoline) emerged as potent in both test series as an effective anticonvulsant agent. Additionally, (8-(3-piperazino)-2-hydroxypropyloxyquinoline) and (8-(3-imidazolo)-2-hydroxypropyloxyquinoline) demonstrated significant anticonvulsant effects in the propanol series, while (8-(2-piperazinoethanoxy)quinoline) and (8-(2-imidazolo-ethanoxy)quinoline) were identified as the most active agents in the ethane series.[5]

ANTHELMINTIC ACTIVITY

2,4-Disubstituted quinolines, supplemented with additional substituents in positions 5–8, exhibit anthelmintic properties. Specifically, 2,4-dimethoxy-6- or 8-arylquinolines have demonstrated potent activity against the sheep nematode Haemonchus contortus, boasting LD99 values comparable to levamisole. Notably, these arylquinolines retain their efficacy even against strains of H. contortus resistant to levamisole, ivermectin, and thiabendazole.[6]

ANT-IMALARIAL ACTIVITY

Malaria, alongside tuberculosis and AIDS, ranks among the most prevalent diseases globally. Compounds containing quinoline, historically employed in malaria treatment dating back to quinine, have undergone extensive research. Charris et al. [910] detailed a series of E-2-quinolinylbenzocycloalcanones 2, examining their efficacy in inhibiting β-hematin formation and haemoglobin hydrolysis in vitro, as well as their effectiveness against rodent Plasmodium berghei. Notably, minimal inhibition of β-hematin formation occurred with hydrogen or methoxy groups at position 8 of the quinoline and position 4' of the indanone ring.[7]

CARDIOVASCULAR ACTIVITY

Quinoline-4-carboxylic acid derivatives were synthesized and evaluated for angiotensin II receptor antagonistic activity and found to be active hypertensive agents .7-substituted or un-substituted 3-acetyl-7, 8-dihydro-2, 5(1H, 6H)-quinolinediones were synthesized and evaluated their inotropic effect.[8]

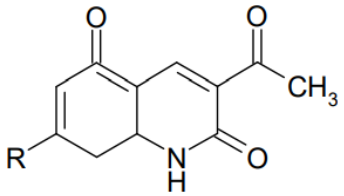

Fig no:4 Quinoline derivative

Table no: 2 Substituents of Quinoline derivatives

S. No	-R
1	$-(CH_2)_3$
2	$-CH_2CH(CH_3)CH_3$
3	$-CH_2C(CH_3)_2CH_3$
4	$-CH_2CH(C_6H_5)CH_3$

6-cyclic aliphatic amino-7-nitro-3,4-dihydroquinoline-2(1H)-one derivatives were synthesized and estimated for platelet aggregation inhibitory effect, cardio tonic action and chonotropic activity and found to be selective platelet aggregation inhibitors and proved that

6-(4-ethoxycarbonylpiperidino)-7-nitro-3,4-dihydroquinoline-2(1H)-one was most potent and highly selective.

ANTI-VIRAL ACTIVITY

Dengue fever, a viral disease experiencing resurgence, poses a significant threat to populations residing in tropical and subtropical regions. Caused by the dengue virus and transmitted by Aedes mosquitoes, the infection proliferates uncontrollably. Classified within the Flavivirus genus of the Flaviviridae family, the dengue virus manifests in four distinct serotypes, lacking long-term cross-protection against subsequent infections. In vitro assessment through the confirmatory viral yield reduction assay revealed that only compounds 1 and 2 consistently exhibited inhibitory activity against DENV2. Compound 1 demonstrated an IC50 of 3.03 µM and a CC50 of 16.06 µM, resulting in an estimated selectivity index (SI) of 5.30. Compound 2 exhibited higher potency with an SI of 39.5, characterized by an IC50 of 0.49 µM and a CC50 of 19.39 µM. [9,10]

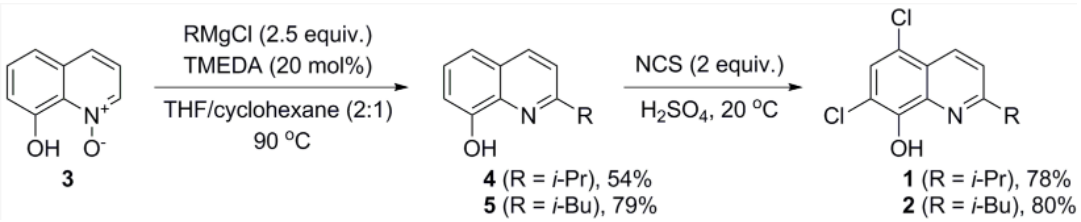

Fig no 5: Synthesis of quinoline derivatives, Compound 1and 2

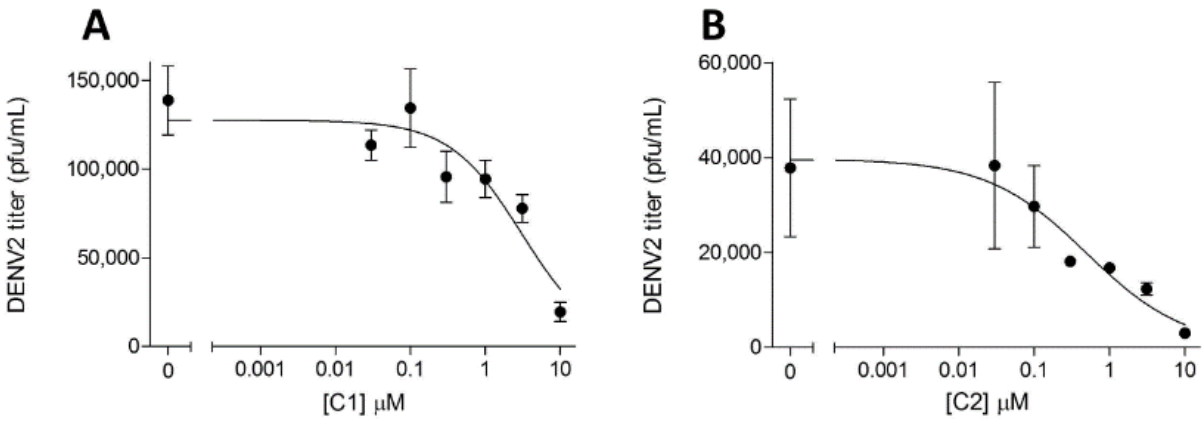

Fig no:6. Quinoline derivatives 1 and 2 are active against DENV2 in a dose-dependent manner.

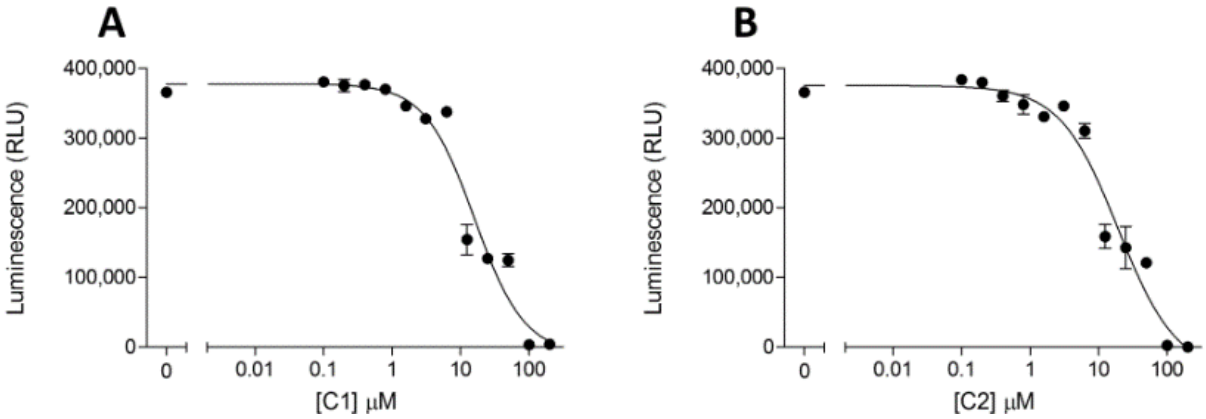

Fig no:7 Cytotoxicity data of compounds 1 and 2 in Vero cells.

CONCLUSION

Quinoline derivatives have proven to be highly effective and potent in a range of pharmacological applications, such as antibacterial, anticancer, antiviral, anti-inflammatory, and antimalarial properties. The pharmacological field is highly promising with quinoline-based compounds because of their wide range of biological activity and possible therapeutic uses. To completely realize their promise in clinical settings, however, more research and development are essential to address issues with safety, resistance, and pharmacokinetics.

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