International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1636-1640 www.ijprajournal.com ISSN: 2456-4494

Design, Synthesis and Insilico Studies of Quinoline Derivatives

Mrs. AnjuJose[1], Beema Ansila Ansari[2], Farsana Sadhik[3]
[1]*Associate Professor Department of Pharmaceutical Chemistry Al Azhar College Of Pharmacy Thodupuzha, Kerala, India*
[2,3]*Students, Al Azhar college of Pharmacy, Thodupuzha, Kerala, India*

Date of Submission: 25-02-2025 Date of Acceptance: 05-03-2025

ABSTRACT
Quinoline, a prominent heterocyclic compound, has emerged as an essential scaffold in the development of new drug entities due to its diverse biological activities. Quinoline and its derivatives have been extensively tested for their efficacy against a range of diseases, making them a valuable class for drug discovery. These compounds have shown significant promise in treating conditions such as anxiety, convulsions, Alzheimer's disease, and Parkinson's disease, among others. The review highlights the natural sources of quinoline and provides insights into quinoline-based drugs that have reached the market. It also explores the biological activities of quinoline derivatives, particularly their neuroprotective and antioxidant properties. In the study, molecular docking simulations were employed to examine the binding affinities of quinoline derivatives with key target proteins involved in these neurological conditions, such as the serotonin 5-HT2A receptor, human carbonic anhydrase II (hCAII), butyrylcholinesterase (BChE), and catechol-O-methyltransferase (COMT). The docking results indicated that several quinoline derivatives demonstrated strong binding affinities and favorable interactions with critical active site residues, suggesting their potential as multi-target inhibitors. Molecular dynamics simulations and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiling further affirmed the stability and pharmacokinetic properties of these compounds, establishing quinoline derivatives as promising candidates for future drug development. These findings offer valuable structural insights that can guide the optimization and advancement of quinoline-based therapeutics for neurodegenerative disorders.

Keywords: Alzheimer's disease, Parkinson disease, Insilico, Moleculardocking, Quinoline, Protein data bank.

I. INTRODUCTION

Quinoline or 1-aza-napthalene or benzo[b]pyridine is nitrogen containing heterocyclic aromatic compound. In 1834, quinoline was first discovered and isolated by Friedlieb Ferdinard Runge from coal tar.[1] It belongs to the alkaloid family and is a secondary metabolite under the nitrogen-containing natural products.[2] It has a molecular formula of C_9H_7N its molecular weight is129.16. Quinoline shows wide varieties of biological activities such as such as antibacterial, anti- fungal, antimycobacterial, antiviral, anti-protozoal, antimalarial, anti- cancer, cardiovascular, CNS effects, antioxidant, anticonvulsant, anti-anxiety, analgesic, anti-inflammatory, anthelmintic and miscellaneous activities.[3]Alzheimer's Disease (AD) is a multifactorial neurodegenerative disorder that leads to cognitive impairments such as memory loss, difficulty in learning, and problems with perception and problem-solving.[4]The disease progression results in abnormal behaviors and severe decline in cognitive abilities. AD is caused by aberrant expression of cholinesterase's (acetylcholinesterase: AChE and butyryl cholinesterase: BChE) and monoamine oxidases (MAO-A and MAO-B).[5,6] Inhibiting the enzyme can raise the level of MAO and AChE in the presynaptic cleft and improve signaling.[7]Choline esterase is found in the central nervous system. It exists in two isoforms acetylcholinesterase (AChE) and butyryl cholinesterase (BChE) [**PDB ID 4DJU**][8]which are responsible for metabolizing AChE into acetic acid and choline, leads to neural cell death.

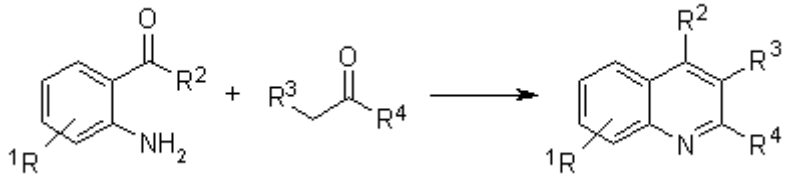
Parkinson disease is a neurodegenerative disorder of aging, characterized by disabling motor symptoms resulting from the loss of midbrain dopaminergic neurons and the decrease of dopamine in the striatum. Levodopa is the single most used drug to treat Parkinson's disease. The enzyme catechol-O-methyltransferase, also known as COMT.Methylation of endogenous catechol-amines, as well as other catechols, is catalyzed by

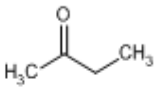
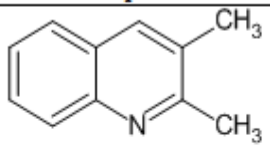
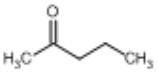
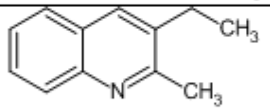
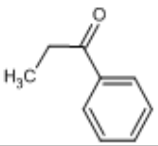
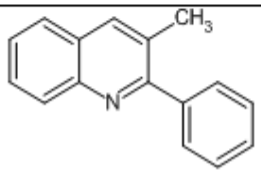
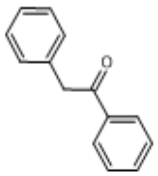
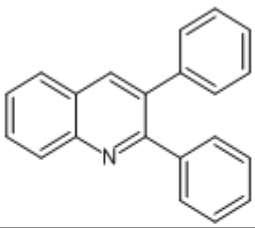
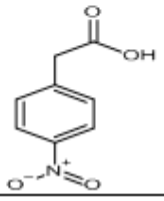
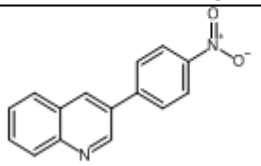
International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1636-1640 www.ijprajournal.com ISSN: 2456-4494

the enzyme catechol-O-methyltransferase (COMT). COMT transfers the methyl group of S-adenosylmethionine (SAM) to the meta- or para-hydroxyl group present in catechols[9,10]De Beer et al. also evaluated by means of molecular docking the affinity of several 3-hydroxypyridin-4-ones that in vitro had displayed high inhibitory activity against COMT **[PDB ID 3BWM],** using the COMT inhibitor 3,5-dinitrocatechol as control.[11]

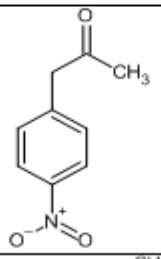
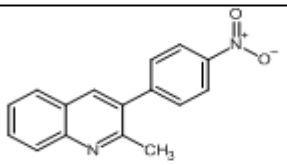
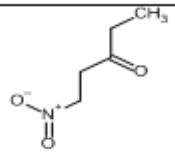
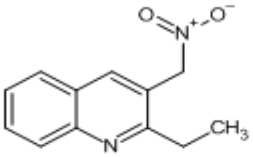
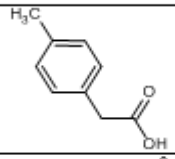
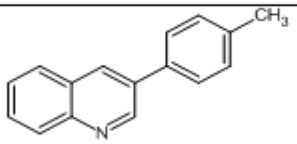
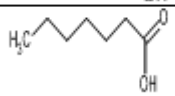
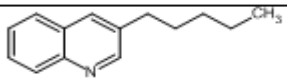
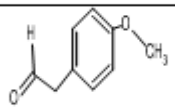
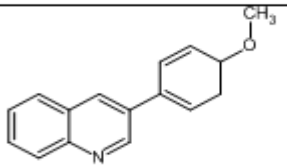
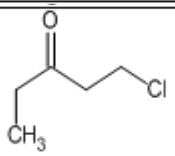
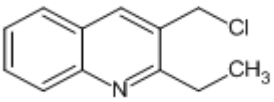
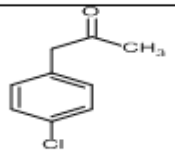
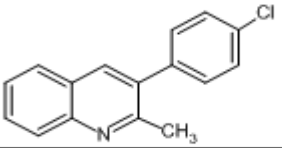
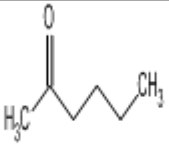
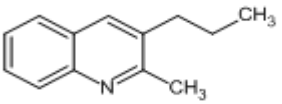
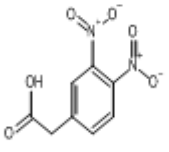
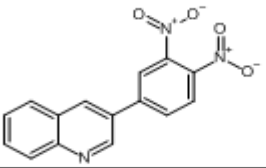
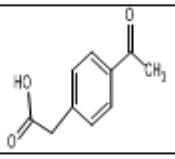
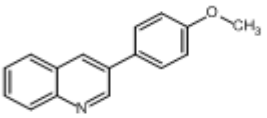
II. MATERIALS AND METHODS

Insilico studies of Quinoline derivatives can be done by using various softwares such as chemsketch, passonline, pkCSM, molsoft and Autodock 1.5 version. Quinoline derivatives synthesized by using friedlanders method .it involve condensation of 2-aminobenzaldehyde and α methyl ketone.(fig:1)



SL NO	R2	Final product
1		
2		
3		
4		
5		

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1636-1640 www.ijprajournal.com ISSN: 2456-4494

6		
7		
8		
9		
10		
11		
12		
13		
14		
15		

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1636-1640 www.ijprajournal.com ISSN: 2456-4494

III. RESULTS AND DISCUSSION

We done the physicochemical properties ,Biologicalactivities,insilico toxicity studies ,pharmacokinetics and docking studies of quinoline derivatives by using various softwares.

We assumed that Q12 (3-(4-chlorophenyl)-2-methylquinoline)do not obey Lipinski's rule so it cannot be used as a druggable derivative. Most of quinoline derivatives act as Taurine dehydrogenase inhibitor, it will provide neuroprotection and anti-oxidant effect. Taurine dehydrogenase inhibitor increases the level of taurine helps to reduce seizure susceptibility and influences mood regulation and cognitive functions.Based on these properties, we can select CNS activity for our studies.In this**,**Q3 (3-methyl 2-phenylquinoline), Q8 (3-(4-methylphenyl)quinoline ,Q14 (3-(3,4-dinitrophenyl)quinoline are highly toxic compounds compared to others.Q14 do not Have BBB permeant so it cannot used as a CNS drug.

MOLECULAR DOCKING STUDIES

- ANTI-ALZHEIMER'S ACTIVITY

Antialzheimers activity of quinoline derivatives can be done by using BChE**[PDB ID :4DJU].**In this study donepezil is used as standard (docking score :-9.4).From the result, Q4 (2,3-diphenylquinoline), Q6(2-methyl-3-(4-nitrophenyl)quinoline) are selected as druggable derivatives due to high docking score.

- ANTI-PARKINSON ACTIVITY

Anti Parkinson activity of quinoline derivatives can be done by using COMT **[PDB ID: 3BWM] .**Levodopa is used as standard in this activity. Docking score is -7.8. From this result, Q4(2,3-diphenylquinoline), Q9 (3-pentylquinoline) are selected as druggable derivatives due to high docking score .

- COMPARISON

Treatment of Neurodegenerative disorder such as Alzheimer's and Parkinson, quinoline derivatives show more inhibiting activity in COMT [PDB ID:3BWM]. So Quinoline derivatives have high effective against Parkinson disease.

IV. CONCLUSION

These projects focused on the in silico molecular docking studies of quinoline derivatives revealed their potential as promising candidates for interacting with the target receptor. Through various computational simulation, we can identify the physiochemical properties, enzyme inhibiting activity, Toxicity studies,ADME properties and drug likeness of quinoline derivatives.The docking results demonstrated favorable binding affinities, suggesting strong interactions through hydrogen bonding, hydrophobic interactions, and

REFERENCES

[1]. R. Alajarin and C. Burgos, Six-membered heterocyles: Quinoline and Isoquinolin, in Heterocyclic Chemistry, ed. J. Alvarez-Builla, J. J. Vaquero and J. Barluenga, John Wiley & Sons, 2011, p. 1527.

[2]. 7 O. Afzal, S. Kumar, M. R. Haider, M. R. Ali, R. Kumar, M. Jaggi and S. Bawa, A review on anticancer potential of bioactive heterocycle quinoline, Eur. J. Med. Chem., 2015, 97, 871–910.

[3]. Matada BS, Pattanashettar R, Yernale NG. A comprehensive review on the biological interest of quinoline and its derivatives. Bioorganic & Medicinal Chemistry. 2021 Feb 15;32:115973.

[4]. M. M. Gonzales, et al., Biological aging processes underlying cognitive decline and neurodegenerative disease, J. Clin. Invest., 2022, 132(10), e158453.

[5]. N. Kumar, et al., Advancements in the development π-π stackingThese studies often reveal that quinoline derivatives exhibit strong binding affinities to key target proteins involved in the pathogenesis of the disorders, such as: Alzheimer's, Parkinson's, Anxiety and Convulsions.of multi- target directed ligands for the treatment of Alzheimer's disease, Bioorg. Med. Chem., 2022, 116742.

[6]. A.U. Syed, et al., Comparison of Monoamine Oxidase-A, Ab Plaques, Tau, and Translocator Protein Levels in Postmortem Human Alzheimer's Disease Brain, Int. J. Mol. Sci., 2023, 24(13), 10808.

[7]. Z.-R. Chen, et al., Role of cholinergic signaling in Alzheimer's disease, Molecules, 2022, 27(6), 1816.

[8]. Shodiq MJ, Hartono F, Khaerunnisa S, Machin A. Analysis of Potential Cinnamomum zeylanicum Blume Essential Oil Against Alzheimer's Disease: A Molecular Docking Study. Pharmacy & Pharmaceutical Sciences Journal/Jurnal Farmasi Dan

IlmuKefarmasian Indonesia. 2023;10(1):111-25.

[9]. P. T. Männisto and S. Kaakkola, "Catechol-O-methyltrans-ferase (COMT): biochemistry, molecular biology, pharma-cology, and clinical efficacy of the new selective COMTinhibitors," Pharmacological Reviews, vol. 51, no. 4pp. 593–628, 1999

[10]. B. Zhu, "Catechol-O-methyltransferase (COMT)-mediatedmethylation metabolism of endogenous bioactive catecholsand modulation by endobiotics and xenobiotics: importancein pathophysiology and pathogenesis," Current Drug Metab-olism, vol. 3, no. 3, pp. 321–349, 2002.

[11]. de Beer, J.; Petzer, J.P.; Lourens, A.C.U.; Petzer, A. Design, synthesis and evaluation of 3-hydroxypyridin-4-ones as inhibitors of catechol-O-methyltransferase. Mol. Divers. 2020, 1–10. [CrossRef]