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REVIEW ARTICLE

1,2,3,4-Tetrahydroquinoline Derivatives and its Significance in Medicinal Chemistry

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ABSTRACT:
1,2,3,4-Tetrahydroquinoline derivatives are the most important class of compounds in the pharmaceutical and agrochemical industries and play important role in the field of medicinal chemistry with so many Pharmacological activities such as anti-cancer, anti-diabetic, anti-parasitic, anti-inflammatory, anti-oxidant, adrenergic, anti-HIV, anti-alzheimer, anti-hyperlipidemic, activities. The tetrahydroquinoline ring containing system found in numerous biologically active natural products and pharmacologically relevant therapeutic agents and very common structure motif. Because of the significance of these scaffolds in medicinal chemistry, the development of some potent and important amalgams continues to be a very active field in development of a promising target for new drug development. 1,2,3,4-Tetrahydroquinoline is one such important part of pharmacophore and having different pharmacological activities. Here we have introduced different 1,2,3,4-tetrahydroquinoline derivatives which possess different biological activities depends on its types and position of substituted functional groups. This review is summarized to know about the chemistry of different 1,2,3,4-tetrahydroquinoline derivatives along with their pharmacological activities.

KEYWORDS: 1,2,3,4-Tetrahydroquinoline, anti-cancer, anti-cancer, anti-diabetic, anti-parasitic, anti-inflammatory.

INTRODUCTION:
Rapid recent developments in the chemistry of 1,2,3,4-tetrahydroquinolines has prompted us to review and classify all their major synthetic methods currently in use. We restrict this report to 1,2,3,4-tetrahydroquinolines in which the C-2, C-3, and C-4 atoms are all sp^3" hybridized.[1]Tetrahydroquinolines is one such important molecular scaffold in medicinal chemistry which serves as an inert carrier for holding various biologically activity. Substituted tetrahydroquinolines are the core structures in many important pharmacological agents and drug molecules, such as anti-arrhythmic and cardiovascular agents, anti-cancer drugs, immunosuppressants, ligands for 5-HT1A and NMDA receptors.[2]

The greatest interest in 1,2,3,4-tetrahydroquinolines is due to their biological activities such as anti-cancer, anti-diabetic, anti-parasitic, anti-inflammatory, anti-oxidant, adrenergic, anti-HIV, anti-alzheimer.

Several of these compounds are naturally occurring like 2-Methyl- 1,2,3,4-tetrahydroquinoline is present in human brain. In fact 2-substituted tetrahydroquinoline Oxamniquine has been used in clinic to treat Manson's schistosomiasis since 1979.[2]Dynemycin, a natural anti-tumor, antibiotic, has a complex structure built on the basis of tetrahydroquinoline system.

Synthesis of 1,2,3,4-tetrahydroquinolines moiety:
Reduction of the heterocyclic ring in quinolones
Direct reduction of the heterocyclic ring can still be the best option for the preparation of tetrahydroquinolines through hydrogenation of quinolones over platinum dioxide in methanol proceeds well under very mild conditions, at room temperature and under atmospheric pressure (**Fig.1**).[1]

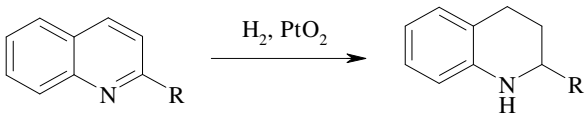

Fig.1

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Conversions of quinolones to 1,2,3,4-tetrahydroquinolines via 1,2-dihydroquinolines

The reaction of quinolone with butyl lithium gives dihydroquinoline, which is then reduced to 2-butyl-1,2,3,4-tetrahydroquinoline in presence of sodium metal in ethanol (**Fig.2**).[1]

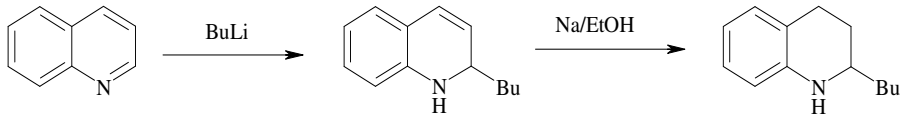
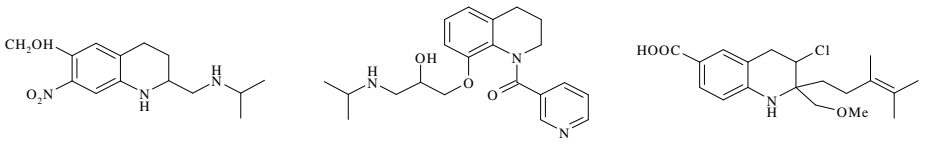


Fig.2

1,2,3,4-Tetrahydroquinoline derivatives available in market:

Many relatively simple synthetic of 1,2,3,4-tetrahydroquinolines are already used or have been tested as potential drugs. Among them Oxamniquine, Nicainoprol have been used as anti -arrhythmic drugs and Virantmycin, a novel antibiotic is the best known example (**Fig.3**).[1]



Oxamniquine **Nicainoprol** **Viratmycin**

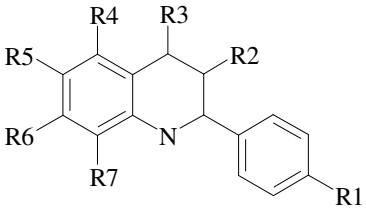
Fig-3

Pharmacology of 1,2,3,4-tetrahydroquinoline derivatives:

1,2,3,4-tetrahydroquinoline have been demonstrated to possess anti-cancer, anti-diabetic, anti-parasitic, anti-inflammatory, anti-oxidant, adrenergic, anti-HIV, anti-alzheimer, anti-hyperlipidemic activities. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities which are given in below literature.

1,2,3,4-Tetrahydroquinoline as anti-cancer agent:

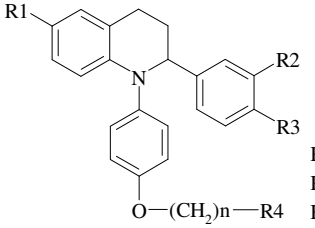
In the recent patent of Raghuram Rao of bio-isosters of quinolones claimed the synthesis of novel 1,2,3,4-tetrahydroquinoline [**1**] with wide varieties of substitution for aromatase enzyme inhibitory activity. These compounds demonstrated mild to moderate aromatase enzyme inhibitory activity in estrogen dependent breast cancer.[3]



R1 = -H, Halo, -(C_1-C_3)alkyl, -O(C_1-C_3)alkyl, -CN
R2 = -H or -(-4-Pyridyl methyl)
R3 = -O-, Heterocycle moiety
R4, R5, R6, R7 = -H, -O(C_1-C_3)alkyl or -CF_3

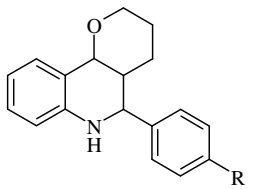
[1]

Wallace *et al* were published a patent on the synthesis of N-substituted 1,2,3,4-tetrahydroquinoline [**2**] and evaluated for its binding, MCF-7 cell-line proliferation. These compounds help to prevent the diseases associated with estrogen hormone like osteoporosis, estrogen dependent breast cancer, endometriosis and uterine fibrosis.[4]



R1 = -OH, -OCH_3
R2 = -OH, -OCH_3
R3 = -OH, -OCH_3
R4 = Pyrrolidine, Piperidine

[2]

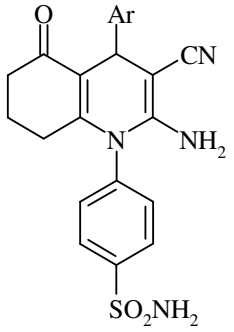


R = -CH_3, -Br, -Cl, -NO_2

[3]

Khan *et al* were synthesized pyrano and furano tetrahydroquinolines [**3**] having different substitution. These derivatives were tested against anti-tumor activity and anti-asthmatic activity.[5]

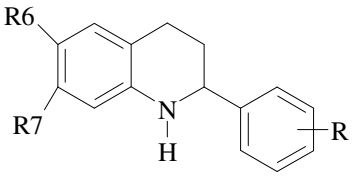
Saleh *et al* studied the synthesis of some novel 4-(2-amino-3-cyano-4-(substituted-aryl)-5-oxo-5,6,7,8-tetrahydroquinolin-1(4H)yl)- benzene sulphonamide [**4**] evaluated for their *in-vitro* anti-tumor activity compared with standard drug like Doxorubicin and assayed for its inhibitory activity of Src protein tyrosine kinases. The Compounds 4c, 4e and 4j with IC50 values are more potent and efficacious than Doxorubicin.[6]



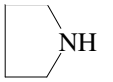
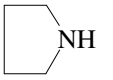
[4]

Comp	Ar
a	$-C_6H_5$
b	$-C_6H_4.CH_3$-4
c	$-C_6H_4.OH$-4
d	$-CH=CH-C_6H_5$
e	$-C_6H_4.OCH_3$-4
f	$-C_6H_4.OCH_3$-2
g	Piperonyl
h	Vanillyl
i	$-C_6H_4.NO_2$-3
j	$-C_6H_4.NO_2$-4

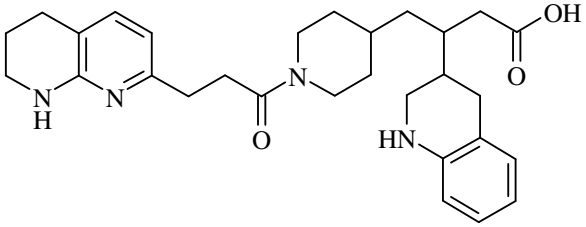
Xia *et al* synthesized a novel series of 6, 7, 2', 3', 4', substituted- 1,2,3,4 tetrahydro-2-phenyl-4-quinolines [**5**] and examined its interactions with tubulin and for cytotoxic activity against a panel of human tumor cell lines including HCT-8, MCF-7, A-549, KB, CAKI-1, SKMEL-2 as anti-tubulin agents.[7]



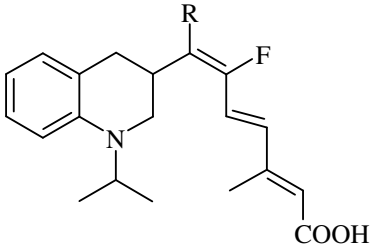
[5]

Comp	R	R6	R7
a	-H	H	H
b	$-OCH_3$	H	H
c	-F	H	H
d	-Cl	H	H
e	-Cl	$-OCH_2O-$	$-OCH_2O-$
f	-F		H
g	-Cl		H

Ghosh *et al* synthesized series of 1, 2, 3, 4- tetrahydroquinoline [**6**] containing $\alpha v\beta_3$ integrin antagonists with superior oral bioavailability. The $\alpha v\beta_3$ integrin is expressed in several cell types such as osteoclasts, endothelial cells, vascular smooth muscle cells and some tumor cells and used for the treatment of cancer, osteoporosis, rhrumatoid arthritis and diabetic retinopathy.[8]



[6]

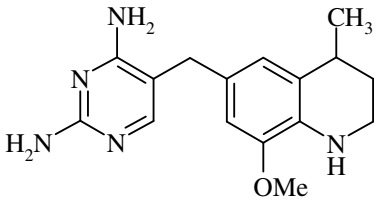


[7]

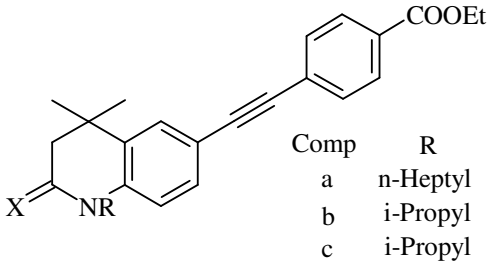
Comp	R
a	H
b	CH_3
c	C_2H_5
d	C_3H_7
e	C_4H_9

Hibi *et al* synthesized a novel series of tetrahydroquinoline derivatives as (E, E, E) -7- (1, 2, 3, 4-tetrahydroquinolin-6-yl)-7-alkyl-6-fluoro-3-methylhepta -2, 4, 6-trienoic acid [**7**] with increases affinity and selectivity for the retinoid X receptors. Addition of fluorine at the 6-position of the 2,4,6-trienoic acid moiety containing compounds which produce potent and selective transactivation of the RXRs.[9]

Rauckman *et al* synthesized library containing a series of eighteen compounds related to tetrahydroquinoline as 2, 4-diamino-5- [(1, 2, 3, 4- tetrahydro-6-quinolyl) methyl] pyrimidines [**8**] and were evaluated as dihydrofolatereductase (DHFR) inhibition. 4-methyl-8-methoxyderivatives showed significant inhibitory activity towards DHFR.[10]



[8]



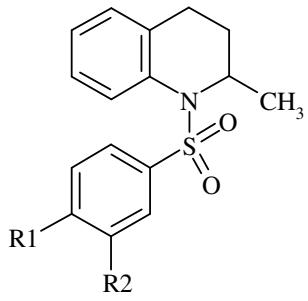
Comp	R	X
a	n-Heptyl	H_2
b	i-Propyl	H_2
c	i-Propyl	O

[9]

Richard *et al* synthesized new tetrahydroquinoline compounds [**9**] from retinoic acid and evaluated as ornithine decarboxylase (ODC) inhibitors. The synthesized ODC inhibitors were examined by binding capacity to the most abundant retinoid receptor RARy in the skin. The compound 9b showed highly potent inhibitors of tumor promoter induced ODC activity in hairless mouse skin.[11]

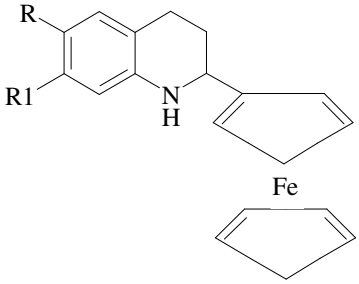
1,2,3,4-Tetrahydroquinoline as anti-parasitic activity:

Romina *et al* synthesized and characterized a novel series of nine new 1-benzenesulfonyl-2-methyl-1,2,3,4-tetrahydroquinoline derivatives [**10**] which tested for anti-parasitic activity against *Trypanozomacruzi*and *Plasmodium falciparum*. The compound 10c demonstrated interesting activity against *Trypanozomacruzi*with low cytotoxicity. The *in-vitro* activities against the protozoan parasites were determined by Benznidazole (*Trypanozomacruzi*) and Chloroquine (*Plasmodium falciparum*).[12]



Comp	R1	R2
a	H	H
b	$NHCOCH_3$	H
c	NO_2	H
d	CH_3	H
e	F	H
f	Cl	H
g	Br	H
h	OCH_3	H
i	H	NO_2
j	NH_2	H

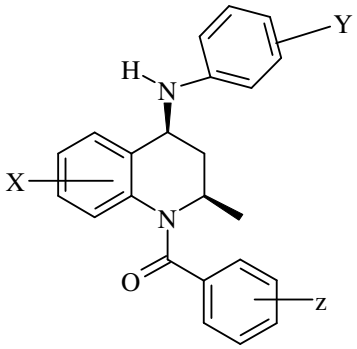
[10]



Comp	R	R1
a	H	H
b	OMe	H
c	H	NMe_2

[11]

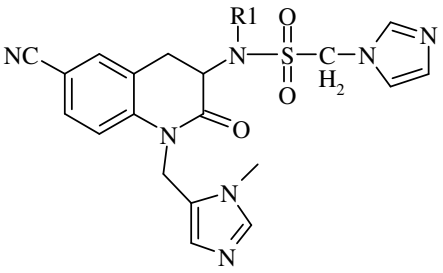
Angela Patti *et al* studied some quinolone based compounds [**11**] bearing a ferrocenyl unit in the 2-position of the heterocyclic system and examined anti-malarial activity. The synthesised ferrocenyl derivatives were evaluated *in-vitro* as anti-malarial agents against Chloroquine-susceptible D10 and Chloroquine-resistant W2 strains of *Plasmodium falciparum.* The compound 11a was showed good activity against the others derivatives.[13]



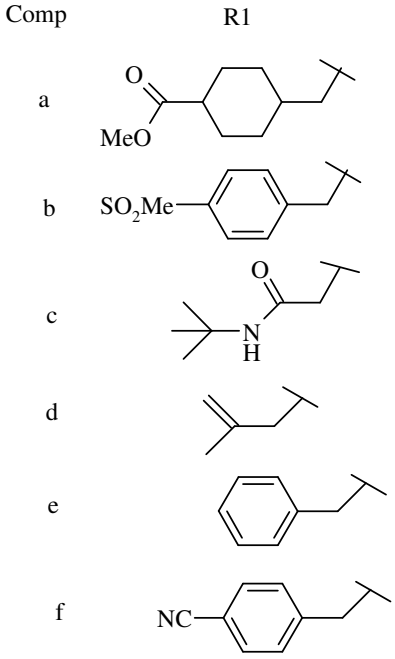
Comp	X	Y	Z
a	H	H	H
b	H	F	2-CH_3
c	F	F	2-CF_3
d	H	F	3-F
e	F	F	4-OCH_3
f	H	CH_3	4-CH_3
g	F	F	3-CF_3

[12]

Smith *et al* synthesized a library of 35 compounds of substituted 1,2,3,4-tetrahydroquinoline as cis -1- benzoyl-2-methyl-4-(phenyl amino)- 1,2,3,4 tetrahydroquinoline derivatives [**12**] and evaluated for their ability to cause expression of a reporter gene downstream of an ecdysone response element in a mammalian cell line engineered to express the ecdysone receptors from Aedesaegypti. The compounds which contain a small lipophilic substituents on the meta and para positions of the benzoyl ring and hydrogen or fluorine at the 4-position of the phenylamino ring and the 6-position of the tetrahydroquinoline ring were the most potent.[14]



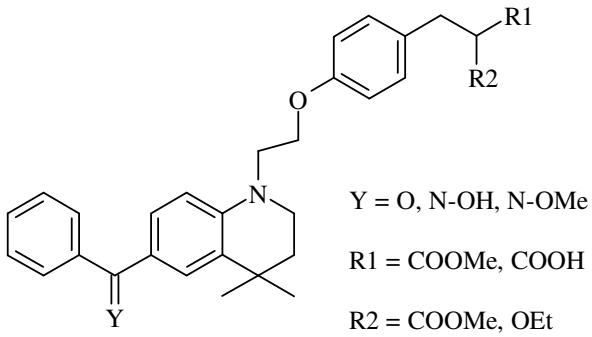
[13]



Vivek *et al* worked on tetrahydroquinoline moiety and synthesised 2-oxo tetrahydroquinoline scaffold [**13**] and evaluated as inhibitors of protein farnesyltransferase. The synthesised derivatives inhibit the growth of the malaria parasite and showed good anti-malarial activity.[15]

1,2,3,4-Tetrahydroquinoline as anti-diabetic agent:

Marie *et al* designed and synthesized novel compound of 4,4-dimethyl-1,2,3,4-tetrahydroquinoline [**14**] as *PPAR* (Peroxisomes Proliferators Activated Receptors) agonists. The compounds were assayed for their ability to prevent Type-2 diabetes and proved to be good *PPAR* agonists. An ether–ester substituent replacing the di-ester function leads to the very partial *PPARa* agonists without lost *PPARc* agonist property.[16]

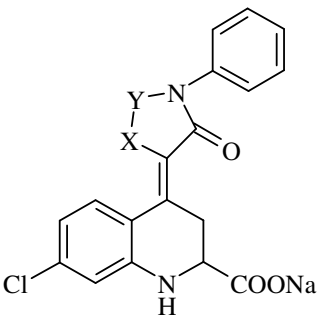


Y = O, N-OH, N-OMe

R1 = COOMe, COOH

R2 = COOMe, OEt

[14]



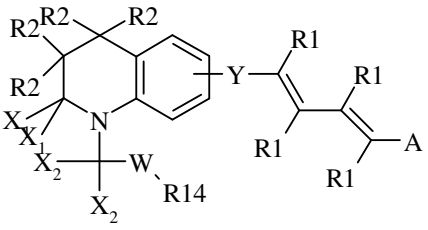
Comp	X	Y
a	CH_2	CH_2
b	CH_2	$(CH_2)_2$
c	CH_2	CO
d	NH	CO

[15]

1,2,3,4-Tetrahydroquinoline as anti-inflammatory agent:

Romano *et al* synthesize the chiral tetrahydroquinoline derivatives [**15**] showing outstanding *in-vivo* anti-hyperalgesic activity in different animal models of sustained inflammation and chronic neuropathic pain by glycine antagonism. The hydantoin derivative 15d was the most potent compound belonging to this sub-series, accounting for additional binding interactions with the receptor site which examined by *in-vitro* binding studies in rat cerebral cortex membranes.[17]

Jayasree *et al* got patent on the synthesis of tetrahydroquinoline derivatives [**16**] having retinoid like activity which use for treating skin-related diseases. These compounds used as agents to treat diseases of the eye, proliferative vitreoretinopathy (PVR), retinal detachment, various cardiovascular diseases, skin related diseases, cancer, and inflammatory diseases.[18]



[16]

X_1 = H or alkyl (C_1 to C_6)

X_2 = Oxo (=O), Thione (=S)

W = $C(R)_2$ where R = R2, Phenyl, Naphthyl

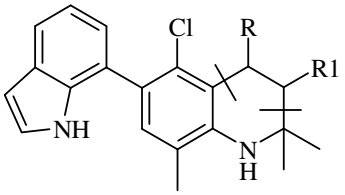
R2 = H, Alkyl (C_1 to C_6), Fluroalkyl (C_1 to C_6)

R3 = H, Alkyl (C_1 to C_6)

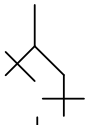
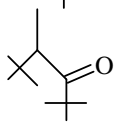
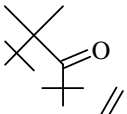
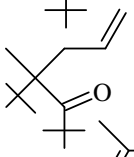
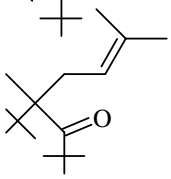
R8 = $-CH_3$, $-C_2H_5$

R14 = H, Alkyl (C_1 to C_{10})

Steven *et al* worked on 6-indole-1,2,3,4-tetrahydroquinolines [**17**] and synthesized a series of glucocorticoid receptor (GR) ligands. The compounds containing the hydroxyl group at C_3 position improving GR selectivity within a series of non-steroidal GR agonists.[19]

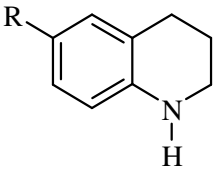


[17]

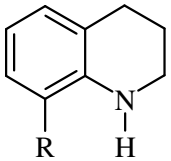
Comp	R + R1
a	Prednisolone
b	
c	
d	
e	
f	

1,2,3,4-Tetrahydroquinoline as anti-oxidant agent:

Nishiyama *et al* reported the synthesis of 1, 2, 3, 4- tetrahydroquinoline derivatives [**18**, **19**] with substitution on C-6 and C-8 positions. The synthesized compounds were screened for anti-oxidant property showed moderate activity. The 1,2,3,4-tetrahydroquinolines with OH and NH_2 groups *ortho* to the heterocyclic NH group had an increased induction period compared to other 1,2,3,4-tetrahydroquinolines.[20]

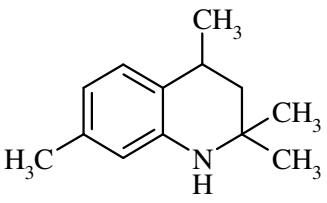


[18]



[19]

Comp.	R
a	H
b	$-C_6H_5$
c	$-OCH_3$
d	-OH
e	-NH

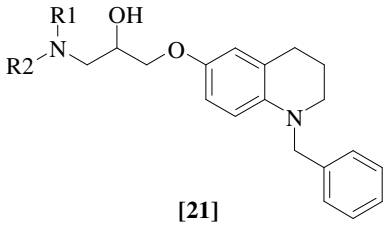


[20]

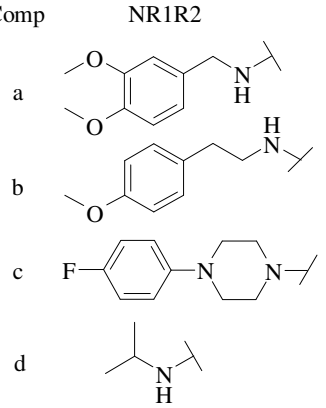
Alina *et al* synthesised 2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline [**20**] is a new synthetic compound with potential anti-oxidant activity. The synthesised compound is structurally similar to Ethoxyquin which is used as an antioxidant and examined the activity on human lymphocytes with the use of the trypan blue exclusion assay, the TUNEL method, the comet assay and the micronucleus test.[21]

1,2,3,4-Tetrahydroquinoline as adrenergic agonist:

Neeraj *et al* studied different derivatives of 1,2,3,4-tetrahydroquinoline [**21**] and evaluated their adrenergic activity. They synthesised a series of novel substituted 1,2,3,4-tetrahydroquinolin-6-yloxypropanes and examined the activity using well established Human SK-N-MC neuroblastoma cells model. The below four derivatives showed good β_3-AR agonistic activity which contained the free OH and NH groups.[22]

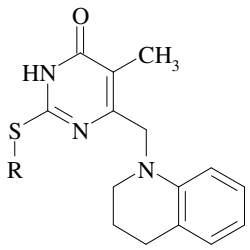


[21]

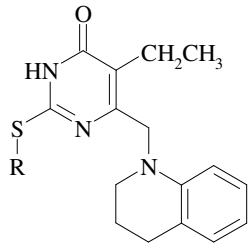


1,2,3,4-Tetrahydroquinoline as anti-HIV agent:

Jing *et al* synthesised novel series of S-DABO analogues of 5-alkyl-2-arylthio-6-((3,4-dihydroquinolin-1(2H)-yl)methyl)pyrimidin-4(3H)-ones [**22**, **23**] and evaluated as inhibitors of human immunodeficiency virus type-1 (HIV-1). Among them, the compounds 22a, 22f, 23a act as most potent HIV-1 inhibitors compared with Nevirapine and Delavirdine.[23]



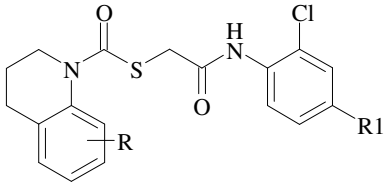
[22]



[23]

Comp	R
a	$PhCOCH_2$
b	$(4'\text{-}CH_3)PhCOCH_2$
c	$(4'\text{-}Cl)PhCOCH_2$
d	$(4'\text{-}NO_2)PHCOCH_2$
e	$(4'\text{-}CN)PhCOCH_2$
f	$(4'\text{-}OCH_3)PhCOCH_2$
g	$(4'\text{-}F)PhCOCH_2$

Dai *et al* synthesized substituted tetrahydroquinoline [**24**] and examined as Non-nucleoside reverse transcriptase inhibitors (NNRTIs). The NNRTIs are key elements of multidrug regimens called HAART (Highly Active Antiretroviral Therapy), which are used to treat HIV-1 infections. The synthesized derivatives showed potent inhibitors of HIV-1 RT.[24]

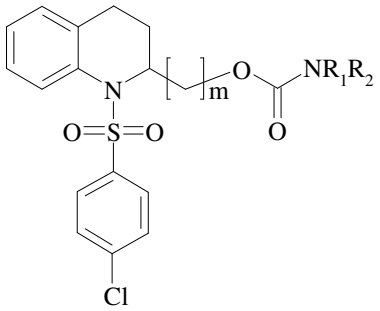


[24]

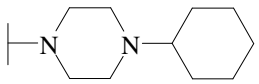
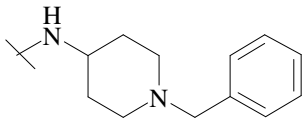
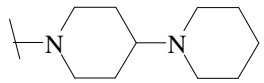
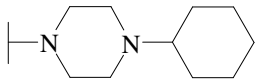
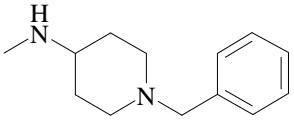
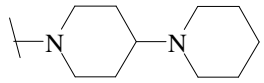
Comp	R	R1
a	6-Me	SO_2NH_2
b	8-Me	SO_2NH_2
c	6-Cl	SO_2NH_2
d	8-Cl	SO_2NH_2
e	6,8-Cl	SO_2NH_2
f	6,8-Cl	H
g	6,8-Cl	CN
h	6,8-Cl	CONHBn
i	6,8-Cl	SO_2CH_3
j	6,8-Cl	$CONH(CH_2)_3NH_2$

1,2,3,4-Tetrahydroquinoline as anti-alzheimer agent:

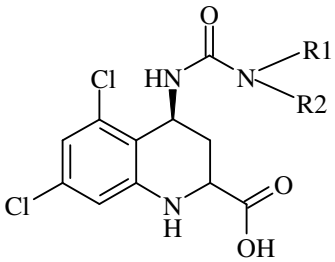
Tao *et al* synthesised tetrahydroquinoline and pyrrolidinesulfonamidecarbamates [**25**] and evaluated as γ-secretase inhibitors. The compound containing piperazine and piperidine with bulky side chains 25(a-c) has higher potency compared to the corresponding two carbon chain carbamates 25(d-f).[25]



[25]

Comp	NR1R2	m
a		3
b		3
c		3
d		2
e		2
f		2

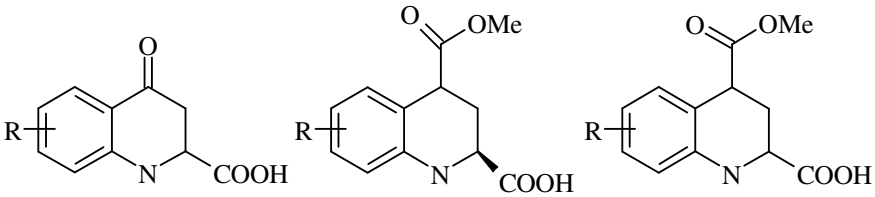
Lesson *et al* reported synthesis of trans-2-carboxy-5,7-dichloro-4-amido tetrahydroquinolines derivatives [**26**] and examined for *in vitro* antagonist activity at the glycine site on the N-methyl-D-aspartate receptor. These compounds showed good anti-alzheimer and anti-parkinsonism activity.[26]



[26]

Comp	R1	R2
a	$-C_6H_5$	H
b	$-CH_2-C_6H_5$	H
c	-1-Napthyl	H
d	$-C_6H_4-CH_3$-4	H
e	$-C_6H_5$	$-CH_3$
f	$-CH_2-C_6H_5$	$-CH_3$
g	$-C_6H_4-CH_3$-3	$-CH_3$
h	$-C_6H_5$	$-C_6H_5$
i	$-CH_2-C_6H_5$	$-C_6H_5$

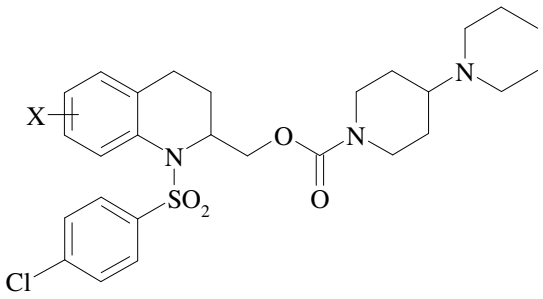
Carling *et al* synthesized derivatives of tetrahydroquinoline as 2- carboxy- 1, 2, 3, 4-tetrahydroquinoline [**27**, **28**, **29**] and evaluated for *in vitro* antagonist activity at the glycine site on the NMDA receptors. The carboxy methyl group to the 4-position responsible for their antagonistic activity.[27]



[27] **[28]** **[29]**

R = -Cl, -Br, -I, -CH_3

Theodros *et al* develop a novel series of tetrahydroquinoline derivatives [**30**] and Screened for γ-secretase inhibitors. The compound **30e** showed potent activity due to Incorporation of a fluorine substituent at the 7-position as compared to other derivatives.[28]

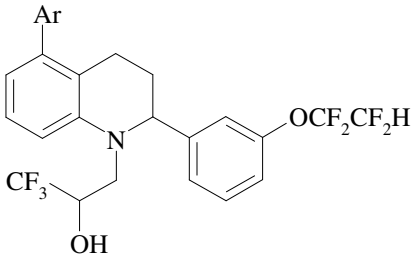


Comp	X
a	H
b	5,7-F_2
c	5,8-F_2
d	6-F
e	7-F

[30]

1,2,3,4-Tetrahydroquinoline as anti-hyperlipidemic agent:

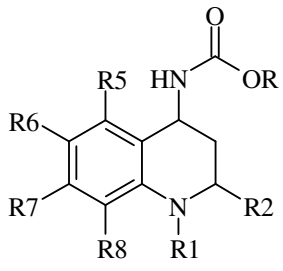
Thomas *et al* synthesized a series of 1,2,3,4-tetrahydroquinoline derivatives [**31**] and evaluated as CETP potent inhibitors. The CETP inhibitors were evaluated by in-vitro studied of purified human plasma derived CETP.[29]



Comp	Ar
a	3-$OCF_3C_6H_4$
b	3-ClC_6H_4
c	3-FC_6H_4
d	3-$OCH_3C_6H_4$
e	3-CNC_6H_4

[31]

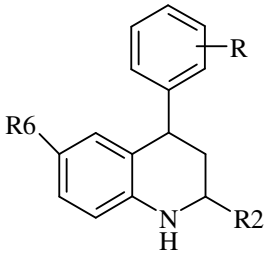
Paul *et al* worked on our interested tetrahydroquinoline ring and prepared 4-protected –amino-2-substituted- 1, 2, 3, 4-tetrahydroquinolines [**32**] as cholesteryl ester transfer protein (CETP) inhibitors. Such inhibitors decrease certain plasma lipid levels and used to treat atherosclerosis and cardiovascular like diseases.[30]



Comp	R	R1	R2	R5	R6	R7	R8
a	CH_3	H	H	H	Cl	H	H
b	C_2H_5	H	H	H	CF_3	H	H
c	C_6H_5	CH_3	H	CH_3	H	H	H
d	C_6H_5	CH_3	H	H	Br	H	H
e	C_6H_5	CH_3	OH	H	NO_2	H	H

[32]

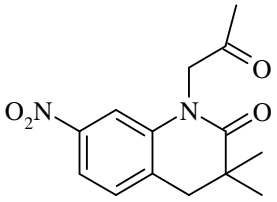
Koutnikova *et al* worked on the tetrahydroquinoline ring and synthesized various 2, 4, 6-substituted derivatives [**33**] for controlling liver-X-receptors activity. The liver-X receptors (LXR-α, LXR-β) are members of the nuclear hormone receptor superfamily of ligand activated transcription factors and have utility in treating or preventing dyslipidemia, skin proliferative disorders, rheumatoid arthritis, cardiovascular diseases and inflammation.[31]



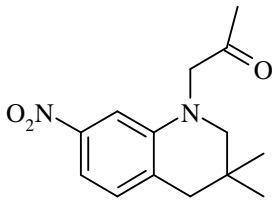
Comp	R	R2	R6
a	4-Cl	C_6H_5	H
b	4-Br	C_6H_5	F
c	4-NO_2	C_6H_5	F
d	4-Cl	C_6H_5	F
e	5-Br	C_6H_5	OCH_3

[33]

Yuzo *et al* synthesized novel 1,2,3,4-tetrahydroquinoline derivatives [**34**,**35**] and evaluated them as Potassium Channel Opener. These derivatives may protect against ischemia and act as anti-lipemic agent also help to lowering low density lipoprotein (LDL) cholesterol while increasing high density lipoprotein (HDL) cholesterol. The compound **35** has potency as Cromakalim and introduction of a carbonyl group to **35** at position 3, as shown in **34**, resulted in a complete loss of activity.[32]



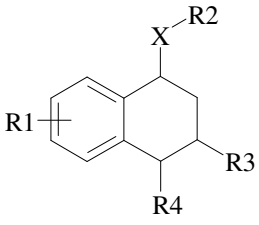
[34]



[35]

1,2,3,4-Tetrahydroquinoline as anti-allergic agent:

Bladh *et al* synthesized a series of derivatives of tetrahydroquinoline [**36**] and their evaluation for modulation of signal transducer and activator of transcription 6 pathways and used in the treatment of allergic asthma, allergic rhinitis, a food allergic, allergic conjunctivies, hayfever, industrial sensitization and COPD.[33]

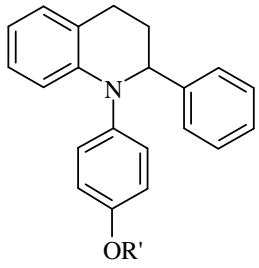


Comp	R1	R2	R3	R4	X
a	6-NO_2	CH_3	H	H	O
b	6-CF_3	CH_3	H	H	O
c	7-OH	C_2H_5	H	H	H
d	7-OH	CH_3	H	H	O
e	8-NO_2	CH_3	H	H	H

[36]

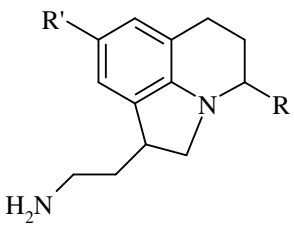
1,2,3,4-Tetrahydroquinoline as anti-fertility agent:

Bell *et al* reported synthesis of diethyl amino ethyl and pyrrolidinyl ethyl ethers of 1-(p-hydroxy phenyl)-2-phenyl – 1, 2, 3, 4-tetrahydroquinolinederivatives [**37**]. These compounds showed good anti-fertility activity.[34]



Comp	R'
a	$-CH_2-CH_2-N-(C_2H_5)_2$
b	$-CH_2-CH_2-N$

[37]



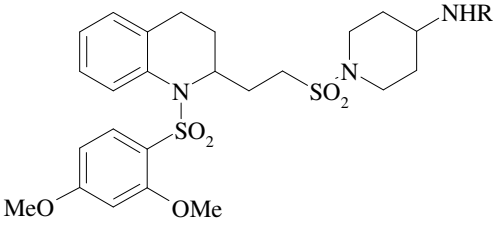
Comp	R	R'
a	H	H
b	CH_3	CH_3

[38]

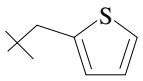
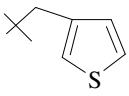
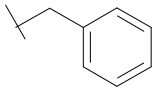
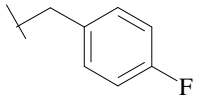
1,2,3,4-Tetrahydroquinoline as anti-psychotic agent

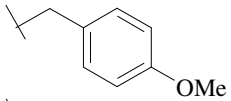
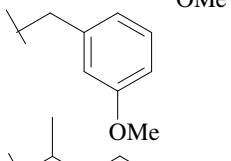
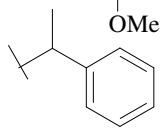
Isaac *et al* synthesized a series of tetrahydroquinoline derivatives as pyrrolo [3, 2, 1] 1, 2, 3, 4-tetrahydroquinoline [**38**] examined them for activity against 5-hydroxy tryptamine receptors (5-HT_{2c} and 5-HT_{2a}). The compounds of this series found to be agonist at 5-HT_{2c} with selectivity over 5-HT_{2a}.[35]

Jack *et al* synthesized a novel series of tetrahydroquinoline sulfonamides derivatives [**39**] as potent and selective Vasopressin 1b (V1b) antagonists. The synthesized derivatives have been postulated as possible treatments for depression and anxiety. The compounds 39e and 39g have low affinity than 39a, 39b and 39c to the receptors.[36]



[39]

Comp	R
a	
b	
c	
d	

Comp	R
e	
f	
g	

CONCLUSION:

Recent developments in the chemistry of 1,2,3,4-tetrahydroquinolines has encouraged us to review with respect to improvised synthetic techniques to prepare numerous tetrahydroquinolines derivatives with regard to their diverse biological and pharmacological applications. Several tetrahydroquinolines having simple or complex substitutions have noteworthy biochemial and pharmacological activities such as anti-cancer, anti-diabetics, anti-inflammatory, anti-oxidant, anti-HIV, anti-alzheimer, anti-hyperlipedemic, anti-psychotic and anti-fertility agents. It reveals that the activity of the 1,2,3,4-tetrahydroquinolines depends on the nature, number and position of the substitution arc the important factors. This review emphasis on the current trends in the synthesis of 1,2,3,4-tetrahydroquinolines for its biological and pharmacological properties.

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