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Advances in the Development of New Bioactive Polyhydroquinolines

Dipti K. Dodiya
Department of Chemistry, H. & H. B. Kotak Institute of Science-Rajkot, Gujarat, India

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ABSTRACT

Quinoline derivatives have been of immense interest due to their wide spectrum biological activity profile. Among quinolines derivatives, polyhydroquinolines including hexahydroquinolines, tetrahydroquinolines, dihydroquinolines etc. have attracted considerable attention from the bioactivity point of view.

The present paper covers a brief report of approaches to newer bioactive polyhydroquinoline derivatives.

Keywords : Polyhydroquinolines, Hexahydroquinolines, Tetrahydroquinolines

I. INTRODUCTION

Quinoline is a heterocyclic scaffold of profound significance to human race. Several quinoline derivatives isolated from natural resources or prepared synthetically are momentous with respect to their biological activity.

Development of new quinoline-based structures has been of immense interest due to their importance as substructures in an extensive range of natural and synthetic products.

Polyhydroquinolines have recently drawn attention due to their attractive bioactivity profile.

Several literature reports have described the preparation and biological evaluation of polyhydroquinolines including hexahydroquinolines, tetrahydroquinolines, dihydroquinolines etc [1, 2].

The present paper reports brief overview of approaches to development of newer polyhydroquinolines and their bioactivity profile.

II. ADVANCES IN DEVELOPMENT OF HEXAHYDROQUINOLINES

Aryl-sulfonamide bearing hexahydroquinolines were designed, synthesized and characterized [3].

The prepared hexahydroquinolines were screened for their anti-cancer potential.

Several compounds from the series displayed good anti-cancer activity in vitro and the results were comparable to that of standard drug. Further, molecular docking studies were conducted into CA-II enzyme site to determine the possible mode of action for the cytotoxicity of the compounds.

Series of novel hexahydroquinoline-carboxylates were prepared and tested for their antihypertensive effect by calcium channel antagonism [4]. Five of the prepared hexahydroquinoline-carboxylates displayed good concentration-dependent activity.

Structure-activity relationships were established for the active compound and it was revealed that methyl carboxylate compounds with halogen substituent on phenyl ring exhibited good activity.

Also, further structural modifications were carried out on the basis of SAR. It was revealed that substituting phenyl ring with pyridine ring enhanced the activity as well.

Zarghi, A. et al. have reported design, preparation and evaluation of anti-inflammatory potential for 5-oxo bearing hexahydroquinoline derivatives [5].

The compounds were particularly assessed for their inhibition potential for cyclooxygenase-2. One compound from the series displayed high inhibition potential with low half maximal inhibitory concentration and good selectivity index.

The compound showed less toxicity and it can serve as a promising lead structure for the development of new anti-inflammatory agents.

Design and preparation of 16 new hexahydroquinolines have been reported. The prepared hexahydroquinolines were screened for their capability as muscle-relaxant and in opening K-channel [6].

The muscle-relaxant activity determined on isolated mass of smooth gastric muscle of rabbits. The results were determined under two test conditions and both the tests revealed that the muscle-relaxant effects were dependent on concentration. Further, several compounds showed the muscle-relaxant effects comparable to that of standard drug pinacidil.

Series of novel trimethoxyphenyl bearing hexahydroquinolines as potential anti-cancer agents has been reported [7]. Several compounds from the series showed good anti-cancer activity comparable to that of the standard drug.

Structure activity relationships were established and it was revealed that trimethoxyphenyl fragment was essential for the activity. Further, the mode of action was determined to be by the inhibition of response of tubulin.

Shahraki et. al. have reported design, preparation, characterization and biological evaluation of new hexahydroquinoline derivatives as potent inhibitors of p-Glycoprotein [8].

The most active compounds from the series were further evaluated using the MTT assay. Structure-activity relationships revealed that presence of 2-nitroaryl at the carbon no. 4 or 4-haloaryl at the carbon no. 2 were essential for the activity.

Further, the compounds did not show any toxic effects on normal cells. Results of molecular simulation studies also supported the experimental findings.

Vanaerschot M. et al. have reported anti-malarial evaluation of novel hexahydroquinolines [9].

The compounds showed good anti-malarial potential against both pathogenic and transmissible intra-erythrocytic forms of the malaria parasite P. falciparum. Their mode of action and efficacy were determined as well.

The disubstituted hexahydroquinolines showed good antibacterial potential. However, none of the compounds from the series showed remarkable anti-fungal activity.

The disubstituted hexahydroquinoline derivatives were also evaluated for their anti-cancer potential.

12 compounds from the series showed remarkable anti-cancer activity against three cancer cell lines. Two most active compounds from these 12 were the most active and they also showed high anti-bacterial potential.

Safak, C.et al. have reported calcium antagonist activity of diversely substituted hexahydroquinoline derivatives [10].

Miri, R. et al. have reported calcium-channel modulatory activity of novel nitroimidazolyl-fragment bearing hexahydroquinolines [11].

Yang, X.-H. et al. have reported design, preparation, characterization of 4-substitutedphenyl bearing hexahydroquinoline as potent anti-oxidant agents [12].

The hexahydroquinolines were evaluated for their capability of scavenging DPPH and ABTS+radicals. The compounds showed good anti-oxidant potential.

Şimşek, R. et al. have reported preparation and calcium antagonistic potential of a series of diversely substituted hexahydroquinolines [13]. The series of 2-alkyl-6,6-dimethyl substituted hexahydroquinolines bearing 4-aryl group were prepared using a facile preparative protocol.

The hexahydroquinoline derivatives did not show remarkable calcium antagonistic potential.

Kısmetli, E. et al. have reported design, preparation and characterization of aminocarbonyl group bearing hexahydroquinoline derivatives [14].

The hexahydroquinoline derivatives were screened for their calcium antagonistic activity on isolated rat ileum artery. Many compounds from the series showed good calcium antagonistic potential.

El-Khouly, A. et al. have reported design, preparation, characterization and biological evaluation of indolyl-fragment bearing hexahydroquinoline derivatives as spasmolytic agents [15].

III. ADVANCES IN DEVELOPMENT OF TETRAHYDROQUINOLINES

Preparation of tetrahydroquinolines bearing nitro group at third position has been reported by Anderson, J. et al. [16].

The new tetrahydroquinolines were prepared from imine and ammonium acetate in diastereoselective way. The cyclization involved nitro-Mannich type of process with intramolecular approach.

Optically active imidazo-fused tetrahydroquinoline derivatives were reported. Their complexes with copper were prepared and their use as effective ligands in the borylation of esters was investigated. This was studied by [17].

Chiral tetrahydroquinolines substituted with amine and hydroxyl groups were synthesized from the starting chiral nitrones [18].

The cycloaddition reaction was intramolecular type. X-ray studies were performed to assign the configuration. The report was submitted by Broggini, G. and group.

Preparation of optically enriched derivatives of tetrahydroquinolines was reported by Maj A. et al. [19]. The study describes hydrogenation of quinolines to prepare tetrahydroquinolines using an asymmetric approach.

In this study, New Iridium-based catalysts were used for asymmetric hydrogenation which were developed in situ. The enantioselective excess was found to be greater than ninety-five percentage.

Novel preparative way was reported by Kouznetsov, V. et al., for quinolines scaffolds, which have been modified at C3 position by diels alder type reaction [20].

This approach exhibited easy and facile synthesis for the preparation of 2,3-disubstituted scaffolds of quinolines by utilising domino-sequential methods and implicating the characteristics of cyclic enol ethers and various amine group bearing aromatic rings, by Diels-Alder type reaction.

Chakraborty, A. et al. have reported conformational studies for Tetarhydroquinolines [21]. The computed studies showed that the highest stability was at S0 and S1 level. Various angles and other geometry of planner structure were considered.

FMO calculations showed the variations in the electron densities at excitation level. In this way the electrostatic interaction and molecular angles, moreover electron affinity was calculated for all the conformers.

Zhou X. F. et al. have reported one study on the photo synthesis approach [22].

The approach describes the preparation of quinolines and tetrahydroquinolines at ambient conditions using photo redox catalyst. The reaction had been found to involve uni-electron transfer and cyclization followed

by intramolecular way. The reaction found to be simple and has ease of approach as compared to traditional synthesis.

One study to give therapeutic approach in lung disease was given by Lu X. Et al. [23]. In that study, they have focused on the natural alkaloid from Labiatae family. Antidesmone is an alkaloid possessing tertahydroquinoline core. The alkaloid was screened biologically in vitro and in vivo for its various effects.

It was revealed that it suppresses function of TNF-α, IL-6 and IL-1β. In vivo studies further revealed its potential for being a good anti-inflammatory agent. Combining these studies, it was concluded that tetrahydroquinoline core containing compounds can be lead structures in development of anti – inflammatory drugs.

Sun N. et al. have reported one study which focussed to explore the RORyt receptors in the treatment of autoimmune disorder [24]. The study reports design, preparation and bioactivity screening of N-sulfonamide bearing tetrahydro derivatives of quinoline.

The molecular modelling and other computational methods were used to design these sequence of tetrahydroquinolines scaffolds containing tertiary sulfonamide with target to enhance the drugability limit by improving metabolites sites. SAR studies further revealed the planned molecules were potent agonists of the receptor.

A new synthetic approach through Povarov method was applied in a study to prepare the tetrahydroquinoline derivatives containing propargyl fragment by Núñez, Y. et al. [25]. The terahydroquinoline derivatives were prepared from anilines functionalized with propargyl using lewis acid catalysts.

The newly prepared tetrahydroquinoline derivatives were screened for their capacity to scavenge free radicals in vitro.

The study revealed that one compound from the series showed good antioxidant effect comparable to the reference vitamin C. Further investigation showed preferable pharmacokinetic advantages for these prepared derivatives, showing their efficacy as potent antioxidants.

Goli N. et al. have reported one study on tetrahydroquinoline derivatives. Various structural modifications were made to the pharmacophore based on tetrahydroquinoline and as a result, total thirty four novel functionalized tetrahydroquinolines were developed [26].

Biological evaluation of these compounds showed the potency of this subjected derivatives as neurotropic agents, which was not highlighted in good amount until this study according to their opinion.

Li, Y. S. et. al. has reported preparation of tetrahydroquinolines bearing arylsubstitution at C2 and furan moiety at C5 were designed and prepared to develop novel inhibitors of phoshodiesterase [27].

The biological evaluation revealed that prepared derivatives have remarkable inhibitory action against lipopolysaccharide and PDe4B. In vivo study on various animal models of asthma showed good activity too.

Strucure-activity relationships were established and it was revealed that compounds containing 4-OCH3-phenyl group showed good inhibiting effect against PDE4B. Molecular docking studies revealed that thesetetrahydroquinolines have π-π stacking interaction with target proteins which enhances the activity.

Duan, C. et al. have reported one study in such a way to obtain the desired tetrahydroquinoline derivatives in stereoselective way [28]. So in aim to investigate that path, an easy approach by applying aza-Michael-Michael reaction was utilized.

The diketoesters and chalcones were condensed to give the diversely substituted tetrahydroquinolines. A wide range of desired products can be gained in this way according the article.

Supranovich, V. et al. have done investigation to give the photochemical approach for preparation of tetrahydroquinoline derivatives by applying photoredox catalyst [29].

In that study blue light over tetrafluoro propyl anilines tends to yield the desired outcome of tetrahydro derivatives of quinoline.

In aim to develop a greener approach, Xin, J. R. et al. have reported one investigation [30]. N-methylanilines with substituted malononitriles were reacted in presence of Rose Bengal to give tetrahydroquinoline derivatives by cyclization and through the tandem radical mechanism.

Corresponding products were obtained with yields of up to 74% under mild conditions. Rose bengal having benefit of low cost and greener with respect to environment, this approach have given good yield. Thus according to their opinion, use of rose bengal catalyst should be explored to carry out this type of reactions.

Novel asymmetric bio catalytic system was gained by incorporating the catalytic amount of rhodium metal and by carrying out hydroxylation in presence of cell medium [31].

This approach allows generation of tetrahydroquinolines having two stereocenters by the hydrogenation of quinolines in good amount of yield using this developed novel catalytic system.

Diaz-Muñoz, G. et al. have given one report on the alkaloids of the type tetrahydroquinoline [32]. Preparation of tetrahydroquinoline alkaloids, was conducted in total three stages yielding good yield and purity.

Preparation involved the uncomman way of witting olefination reaction using phase transfer pathway to give ylides which were reacted with carbonyls to give the tertahydroquinlines. The pathway can be further extended to give diversely substituted terahydroquinolines.

An investigation have been done by Castillo, J. et al. to develop a novel synthetic prorocol without the use of catalyst [33]. Sequence of Domino Mannich and methylation generated the desired tetrahydroquinolines.

The prepared derivatives by this approach were screened for their anticancer activity.

In that screening, one compound displayed good potential when tested against fifty seven different cancer cell lines. Further studies revealed that the mechanism of action of the active compound was through suppressing progression of cell cycle. Thus, it was revealed that compounds can act as lead in the search of good antiproliferative agents.

Madhuban, M. et al. have submitted report describing enantiospecific way towards preparation of tetrahydroquinoline alkaloids [34]. The report claimed to have good amount of desired results from the corresponding starting materials.

A novel preparation was reported by research group by taking novel amine-squaramides as catalysts [35]. The developed catalysts were modified with alkoxy chains. They were found to be effectively catalysing the asymmetric reaction in medium containing CO2 at lower pressure and room temperature for the preparation of tetarhydroquinolines.

Two types of diversely substituted optically active alkoxy-containing tetarhydroquinolines were synthesized. This process had given proficient amount of product.

Sheikhhosseini, E. et al. have done one investigation for the preparation of amine bearing tetrahydroquinolines [36].

The preparation consisted of two steps. In the intial stage, the bis-arylidene substituted cycloalkanone were reacted with Propanedinitrile to give the corresponding pyrans, which were then converted to corresponding tetrahydroquinolines using ammonium acetate.

The study done by research group showed novel and simple preparative route for the tetrahydroquinoline derivatives [37]. In that study, Diacetate of Ethylene-diamine was used as catalyst in the cyclization of benzaldehyde bearing amine group with dicarbonyls.

The study has reported an easy approach for the preparation of tetrahydroquinolines.

A novel approach for the preparation of novel tetrahydroquinolines have been reported by Yadav, J. S. et al. [38]. Cyclization of aromatic amine with d-glycals in the presence of cerium chloride and sodium iodide in moderate reaction conditions to give new tetrahydroquinoline.

The protocol has given good amount of product with efficient stereoselectivity. The stereochemistry of synthesized compounds was confirmed using NMR analysis.

Goujon, J. Y. et al. have carried out one study to form tetrahydroquinoline derivatives from epoxy bearing alcohols [39].

Simple approach for developing optically active tetrahydroquinoline substances by doing epoxidation of allylic alcohols through intermolecular pathway is descibed.The structures were confirmed by the NMR studies.

Palaniappan, S. et al. have done study on preparing the geometrical isomers of furano- and pyrano-fused derivatives of tetrahydroquinolines [40].

These derivatives were prepared by polymer based solid catalyst. By performing aza-Diels-Alder one pot reaction of arylaldehydes, dihydro pyran and aryl amines, pyrano fused quinolines were obtained.

The reaction was catalysed easily by the newly developed polymeric solid catalyst at normal condition and even in solvent less approach. The change in temperature gave rise to the trans isomer according to the study.

Use of furan instead of dihydropyran generated furano- fused quinolines were generated almost exclusively in cis form.

This reaction possessed all the advantages of green chemistry as it has furnished high yields and the no use of solvent lead it to be the more favourable in terms of green chemistry. The study claimed that the the protocol provided economic alternative with less time-consumption and lower amount of work up needed to obtain the product.

Rafiee, E. et al. have reported novel preparation of tetrahydroquinlines from various carbohydrate derivatives [41]. The preparation was carried out by reaction of D-arabino-Hex-1-enitol with different anilines in the presence of dodecatungstocobaltate.

The reaction did not involve any drastic reaction conditions and did not require longer reaction hours as well. Hence, the method was mild and provided an efficient access to structurally diverse tetrahydroquinolines.

IV. ADVANCES IN DEVELOPMENT OF POLYHYDROQUINOLINES

Novel disubtituted polyhdyroquinolines were designed, synthesized and screened for their antidiabetic as well lipid lowering activity [42].

Many compounds from the series displayed promising antidiabetic activity on three different types of rat models in vivo. Further, the compounds were also screened in different models in vitro find out the plausible mode of action of the active compounds.

Some of the compounds were found to be inhibiting the PTP while some others were found to be inhibiting GC-phosphorylase. So the compounds were found to be acting via different mode of action surprisingly.

Novel pyrazino- and diazepino- fused polyhydroquinolines have been prepared by Schrader, T. O. et al. [43]. The preparation of optically active polyhydroquinoline derivatives was carried out using lithiation as a key step.

The cyclization was then followed using an intramolecular substitution nucleophilic reaction to give the fused polyhydroquinolines.

Microwave-assisted preparation of heterocycle substituted polyhydroquinolines have been reported [44]. The preparation involved reaction of 5,5-Dimethylcyclohexane-1,3-dione, Ethyl 3-oxobutanoate, tetrazoloquinoline aldehyde and NH4OCOCH3.

The preparation gave fast, facile, environmental friendly access to heterocycle substituted polyhydroquinolines in good yields.

All the synthesized heterocycle substituted polyhdyroquinolines were evaluated for their antibacterial and antifungal activity. Many compounds from the series showed good antibacterial and antifungal potential.

Raouf H. et. al. have developed a novel copper (II) complex based catalyst for development of polyhydroquinolines through Hantzsch protocol [45]. This catalyst is reusable and has been proved efficient for carrying out Hantzsch reaction using various substrates and solvents. It has also showed good catalytic efficiency for solvent-free protocol as well.

V. REFERENCES

[1]. Abdelmoniem, A., Mohamed, M., Abdelmoniem, D., Ghozlan, S., Abdelhamid, I.. (2019). Recent Synthetic Approaches and Biological Evaluations of Amino Hexahydroquinolines and Their Spirocyclic Structures. Anticancer Agents Med Chem., 19(7):875-915.

[2]. Sabale, P. Kaur, P. (2013). 1,2,3,4-Tetrahydroquinoline Derivatives and its Significance in Medicinal Chemistry, Asian J. Research Chem. 6(6): 599-610.

[3]. Mansour, S., Mostafa, M., Mohammed, S. and Mostafa, M., Synthesis and in vitro anticancer evaluation of some novel hexahydroquinoline derivatives having a benzenesulfonamide moiety. (2011). European Journal of Medicinal Chemistry, 46: 201-207.

[4]. Rahime, Ş., Burçin, İ. And İnci, S. (2000). Synthesis and calcium antagonistic activity of 2,6,6-trimethyl-3-carbomethoxy(ethoxy)-4-aryl-1,4,5,6,7,8-hexahydroquinoline derivatives. Il Farmaco, 55: 665-668.

[5]. Zarghi, A., Sabakhi, I., Topuzyan, V., Hajimahdi, Z. and Daraie, B. (2014). Design, synthesis and biological evaluation of 5-oxo-1,4,5,6,7,8 hexahydroquinoline derivatives as selective cyclooxygenase-2 inhibitors. Iran J Pharm Res, 13: 61-65.

[6]. Miyase, G., Gökçe, S., Rahime, Ş. And Cihat, Ş. (2008). Evaluation of myorelaxant activity of 7-substituted hexahydroquinoline derivatives in isolated rabbit gastric fundus. European Journal of Medicinal Chemistry, 43: 562-568.

[7]. Saleh, I., Areej, M., Ahmed, M. and Mostafa, M. (2009). Synthesis and biological evaluation of 2-amino-7,7-dimethyl 4-substituted-5-oxo-1-(3,4,5-trimethoxy)-1,4,5,6,7,8-hexahydro-quinoline-3-carbonitrile derivatives as potential cytotoxic agents. Bioorganic & Medicinal Chemistry Letters, 19: 6939-6942.

[8]. Shahraki, O., Edraki, N., Khoshneviszadeh, M. and Zargari, F. (2017). Novel 5-oxo-hexahydroquinoline derivatives: design, synthesis, in vitro P-glycoprotein-mediated multidrug resistance reversal profile and molecular dynamics simulation study. Drug Des Dev Therapy, 11: 407-412.

[9]. Vanaerschot, M., Lucantoni, L., Li, T., Combrinck, J. M. and Ruecker, A. (2017). Hexahydroquinolines are antimalarial candidates with potent blood-stage and transmission-blocking activity. Nat Microbiol, 2: 1403.

[10]. Safak, C., Erdemli, I. and Sunal, R. (2003). Synthesis of some 1,4,5,6,7,8-hexahydroquinoline derivatives and their calcium antagonistic activity. Arzneimittelforschung, 43: 1052–1055.

[11]. Miri, R., Javidnia, K., Mirkhani, H., Hemmateenejad, B. and Sepeher Z. (2007). Synthesis, QSAR and calcium channel modulator activity of new hexahydroquinoline derivatives containing nitroimidazole. Chem. Biol. Drug Des., 70: 329–336.

[12]. Yang, X.-H., Zhang, P.-H., Zhou, Y., Liu, C., Lin, X. (2011). Synthesis and antioxidant evaluation of novel 4-aryl-hexahydroquinolines from lignin. Arkivoc, 10: 327–337.

[13].Şimşek, R., Şafak, C., Erol, K. and Sirmagül, B. (2001). Studies on calcium antagonist activities of 2-ethyl-3-carbmethoxy-4-aryl-5-oxo-6,6-dimethyl-1,4,5,6,7,8-hexahydroquinoline derivatives. Arzneimittelforschung, 51: 959–963.

[14].Kısmetli, E., Şafak, C., Erol. K., Sırmagül, B. and Linden, A. (2004). Studies on 3-diethyl-aminocarbonyl-1,4,5,6,7,8-hexahydroquinoline derivatives and their calcium channel antagonistic activities in vitro. Arzneimittelforschung, 54: 371–375.

[15].El-Khouly, A., Gündüz, M., Cengelli, C., Şimşek, R. and Erol, K. (2013). Microwave-assisted synthesis and spasmolytic activity of 4-indolylhexahydroquinoline derivatives. Drug Res, 63: 579–585.

[16].Anderson, J. C., Noble, A. and Torres, P. R. (2012). An intramolecular nitro-Mannich route to functionalised tetrahydroquinolines. Tetrahedron Letters, 53(42): 5707-5710.

[17].Zhang, S., Hu, D. B., He, J. B., Guan, K. Y. and Zhu, H. J. (2014). A novel tetrahydroquinoline acid and a new racemic benzofuranone from Capparis spinosa L., a case study of absolute configuration determination using quantum methods. Tetrahedron, 70(4): 869-873.

[18].Broggini, G., Colombo, F., De Marchi, I., Galli, S., Martinelli, M. and Zecchi, G. (2007). Synthesis of enantiopure 4-amino-3-hydroxymethyl-tetrahydroquinolines via an intramolecular nitrone cycloaddition. Tetrahedron: Asymmetry, 18(12): 1495-1501.

[19].Maj, A. M., Suisse, I., Hardouin, C. and Agbossou-Niedercorn, F. (2013). Synthesis of new chiral 2-functionalized-1, 2, 3, 4-tetrahydroquinoline derivatives via asymmetric hydrogenation of substitutedquinolines. Tetrahedron, 69(44): 9322-9328.

[20].Kouznetsov, V. V., Gómez, C. M. M., Ruíz, F. A. and Olmo, E. (2007). Three-component imino Diels–Alder reaction with essential oil and seeds of anise: generation of new tetrahydroquinolines. Tetrahedron Letters, 48(50): 8855-8860.

[21].Chakraborty, A. and Das, L. (2017). Conformational landscape, stability, potential energy curves and vibrations of 1, 2, 3, 4 tetrahydroquinoline. Journal of Molecular Structure, 1136: 80-89.

[22].Zhou, X. F., Sun, Y. Y., Dai, J. J., Xu, J. and Xu, H. J. (2018). Photoinduced synthesis of quinoline derivatives catalyzed by organic photocatalyst at room temperature. Journal of Photochemistry and Photobiology A: Chemistry, 355: 186-193.

[23].Lu, X., Pu, Y., Kong, W., Tang, X., Zhou, J., Gou, H. and Shen, J. (2017). Antidesmone, a unique tetrahydroquinoline alkaloid, prevents acute lung injury via regulating MAPK and NF-κB activities. International immunopharmacology, 45: 34-42.

[24].Sun, N., Ma, X., Zhou, K., Zhu, C., Cao, Z., Wang, Y. and Fu, W. (2020). Discovery of novel N-sulfonamide-tetrahydroquinolines as potent retinoic acid receptor-related orphan receptor γt inverse agonist for the treatment of autoimmune diseases. European Journal of Medicinal Chemistry, 187: 111984-111987.

[25].Núñez, Y. A. R., Norambuena, M., Bohorquez, A. R. R., Morales-Bayuelo, A. and Gutíerrez, M. (2019). Efficient synthesis and antioxidant activity of novel N-propargyl tetrahydroquinoline derivatives through the cationic Povarov reaction. Heliyon, 5(8): e02174-e02181.

[26].Goli, N., Mainkar, P. S., Kotapalli, S. S., Tejaswini, K., Ummanni, R. and Chandrasekhar, S. (2017). Expanding the tetrahydroquinoline pharmacophore. Bioorganic & Medicinal Chemistry Letters, 27(8): 1714-1720.

[27].Li, Y. S., Liu, X. Y., Zhao, D. S., Liao, Y. X., Zhang, L. H., Zhang, F. Z. and Cui, Z. N. (2018). Tetrahydroquinoline and tetrahydroisoquinoline derivatives as potential selective PDE4B inhibitors. Bioorganic & Medicinal Chemistry Letters, 28(19): 3271-3275.

[28].Duan, C., Yao, Y., Ye, L., Shi, Z., Zhao, Z. and Li, X. (2018). Highly stereoselective construction of tetrahydroquinolines via cascade aza-Michael-Michael reaction: Formal [4+2] cycloaddition of β, γ-unsaturated α-ketoesters with 2-aminochalcones. Tetrahedron, 74(50): 7179-7185.

[29].Supranovich, V. I. and Dilman, A. D. (2019). Synthesis of tetrafluorinated

[30].tetrahydroquinolines via photoredox catalysis. Mendeleev Communications, 29(5): 515-516.

[31].Xin, J. R., Guo, J. T., Vigliaturo, D., He, Y. H. and Guan, Z. (2017). Metal-free visible light driven synthesis of tetrahydroquinoline derivatives utilizing Rose Bengal. Tetrahedron, 73(31): 4627-4633.

[32].Wang, J., Li, K., Zhou, X., Han, W., Wan, N., Cui, B. and Chen, Y. (2017). Asymmetric combinational "metal-biocatalytic system": One approach to chiral 2-subsituted-tetrahydroquinoline-4-ols towards two-step one-pot processes in aqueous media. Tetrahedron Letters, 58(23): 2252-2254.

[33].Diaz-Muñoz, G., Isidorio, R. G., Miranda, I. L., de Souza Dias, G. N. and Diaz, M. A. N. (2017). A concise and efficient synthesis of tetrahydroquinoline alkaloids using the phase transfer mediated Wittig olefination reaction. Tetrahedron Letters, 58(33): 3311-3315.

[34].Castillo, J. C., Jiménez, E., Portilla, J., Insuasty, B., Quiroga, J., Moreno-Fuquen, R. and Abonia, R. (2018). Application of a catalyst-free Domino Mannich/Friedel-Crafts alkylation reaction for the synthesis of novel tetrahydroquinolines of potential antitumor activity. Tetrahedron, 74(9): 932-947.

[35].Madhuban, M. V., Shankar, R., Krishna, T., Kumar, Y. S., Chiranjeevi, Y., Muralikrishna, C. and Akula, R. (2017). A convergent approach towards the synthesis of the 2-alkyl-substituted tetrahydroquinoline alkaloid (–)-cuspareine. Tetrahedron: Asymmetry, 28(12): 1803-1807.

[36].Filatova, E. V., Turova, O. V., Nigmatov, A. G. and Zlotin, S. G. (2018). Green asymmetric synthesis of tetrahydroquinolines in carbon dioxide medium promoted by lipophilic bifunctional tertiary amine–squaramide organocatalysts. Tetrahedron, 74(1): 157-164.

[37].Sheikhhosseini, E., Farrokhi, E. and Bigdeli, M. A. (2016). Synthesis of novel tetrahydroquinoline derivatives from α, α′-bis (substituted-benzylidene) cycloalkanones. Journal of Saudi Chemical Society, 20: S227-S230.

[38].Lee, Y. R. and Hung, T. V. (2008). Ethylenediamine diacetate (EDDA)-catalyzed one-pot synthesis of tetrahydroquinolines by domino Knoevenagel/hetero Diels–Alder reactions from 1, 3-dicarbonyls. Tetrahedron, 64(30-31): 7338-7346.

[39].Yadav, J. S., Reddy, B. V. S., Srinivas, M. and Padmavani, B. (2004). CeCl3· H2O/NaI-Promoted stereoselective synthesis of 2, 4-disubstituted chiral tetrahydroquinolines. Tetrahedron, 60(14): 3261-3266.

[40].Goujon, J. Y., Zammattio, F., Chrétien, J. M. and Beaudet, I. (2004). A new approach to 2, 2-disubstituted chromenes and tetrahydroquinolines through intramolecular cyclization of chiral 3, 4-epoxy alcohols. Tetrahedron, 60(18): 4037-4049.

[41].Palaniappan, S., Rajender, B. and Umashankar, M. (2012). Controllable stereoselective synthesis of cis or trans pyrano and furano tetrahydroquinolines: Polyaniline-p-toluenesulfonate salt catalyzed one-pot aza-Diels–Alder reactions. Journal of Molecular Catalysis A: Chemical, 352: 70-74.

[42].Rafiee, E. and Azad, A. (2007). Cobaltpolyoxometalate-catalyzed cyclization of glucal with aryl amines: Synthesis of 2, 4-disubstituted tetrahydroquinolines. Bioorganic & Medicinal Chemistry Letters, 17(10): 2756-2759.

[43].Kumar, A., Sharma, S., Tripathi, V. D., Maurya, R. A., Srivastava, S. P., Bhatia, G., & Srivastava,

A. K. (2010). Design and synthesis of 2, 4-disubstituted polyhydroquinolines as prospective antihyperglycemic and lipid modulating agents. Bioorganic & Medicinal Chemistry, 18(11): 4138-4148.

[44]. Schrader, T. O., Kasem, M., Sun, Q., Wu, C., Ren, A. and Semple, G. (2016). Complementary asymmetric routes to fused tricyclic (R)-2, 3, 4, 4a, 5, 6-hexahydro-1H-pyrazino [1, 2-a] quinolines and (R)-1, 2, 3, 4, 5, 5a, 6, 7-octahydro-[1, 4] diazepino [1, 2-a] quinolines. Tetrahedron Letters, 57(42): 4730-4733.

[45]. Ladani, N. K., Mungra, D. C., Patel, M. P., and Patel, R. G. (2011). Microwave assisted synthesis of novel Hantzsch 1, 4-dihydropyridines, acridine-1, 8-diones and polyhydroquinolines bearing the tetrazolo [1, 5-a] quinoline moiety and their antimicrobial activity assess. Chinese Chemical Letters, 22(12): 1407-1410.

[46]. Raouf, H., Allameh, S., Beiramabadi, S. A., Morsali, A. (2018). An Efficient and Facile Synthesis of Polyhydroquinolines through Hantzsch Reaction Catalyzed by a Novel and Reusable Cu (II) Complex. J Biochem Tech, 9(1):61-64.

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