World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Synthesis and *in vitro* anticancer activity of novel 1,4-dimethyl-9-*H*-carbazol-3-yl) methanamine derivatives against human glioma U87 MG cell line

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World Journal of Advanced Research and Reviews, 2023, 19(01), 1099–1108

Publication history: Received on 08 June 2023; revised on 18 July 2023; accepted on 20 July 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.19.1.1446

Abstract

Glioblastoma Multiforme (GBM) is most aggressive type of brain tumor in adults. 1,4-dimethyl carbazoles exhibits significant anticancer activities in literature. In this research article, we synthesized a series of novel 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine and its derivatives (13-24) and evaluated their *in vitro* cytotoxicity activities against human glioma U87 MG cell line using MTT assay for 24 h phase time period. All final carbazole derivatives were well confirmed by NMR and HRMS spectroscopy techniques. In series, few compound (**15-17**) found excellent *in vitro* anticancer activity (IC_{50}) values 18.50 µM, 47 µM and 75 µM respectively against human glioma U87MG cell line compare to standard drugs used in brain cancer such as Carmustine (IC_{50} = 18.24 µM) and Temozolomide (IC_{50} = 100 µM) respectively. Among these derivatives, compound **15** was found to have the most potent cytotoxic effect on tested glioma cell line. This study supported that 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine derivatives found significant anticancer potential against human glioma U87MG cell line.

Keywords: Carbazole; Anticancer; Glioma; MTT (3-(4,5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide)

1. Introduction

Gliomas/glial tumors are primary brain tumors arising from glial cells, which form the supporting tissue of the nervous system [1]. Glioblastoma Multiforme (GBM): This is most aggressive form of brain tumor in adults [2, 3,4]. Current median length of survival for GBM patients is around 12-14 months [3,4, 5]. Current treatment therapy is not sufficient for glioma treatment [5,6]. However, common treatment approach for glioma is surgery, combined with radiotherapy and chemotherapy [5, 6]. Majority of malignant brain tumors are incurable, the combined therapy can significantly prolong survival and also palliative support [3,4].

Carbazole, a N-nitrogen containing tricyclic compound present naturally as well as chemically synthesized showed potential anticancer activities in literature [7-9]. Carbazole structure-based compounds are frequently found in anticancer lead discovery [7-9]. Midostaurin, an anticancer drug based on carbazole structure (Novartis), used in treatment of newly diagnosed acute myeloid leukemia (AML) and for advanced systemic mastocytosis [9, 10]. The diverse biological activities of carbazole derivatives are related to the presence of planar structure which interact with DNA either via intercalation between base pairs or electrostatic interaction in the minor or major groove[11,12]. Pyridocarbazole structure based a Celiptium drug is being commercialized in France market for treatment for metastatic breast cancer(Sanofi France group) [4, 13]. 1,4-dimethyl-9-*H*-carbazole structure is the part of ellipticine (**1**). In review literature survey, 1,4-dimethyl-carbazole derivatives target STAT3 (Signal transducers and activators of transcription) protein. STAT3 is a major target for the development of novel cancer therapeutics [14]. 1,4-dimethyl-carbazoles also showed potential anticancer and anti-HIV activity[14-16]. Carbazole structure is also present in

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vincristine (**2**), vinblastine isolated from the Madagascar periwinkle Catharanthus roseus also used in glioblastoma treatment [12, 17-18]. Vincristine (**2**) also used in various cancer diseases like acute lymphocytic leukemia acute myeloid leukemia, Hodgkin's disease, neuroblastoma and small cell lung cancer [17, 18]. Most anticancer drugs, whether synthetic chemicals or natural products, interact with DNA or its precursors, and cause irreversible damage to DNA and inhibit the synthesis of new genetic materials.

1.1. Rational approach for designed novel 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine derivatives

Pyridocarbazole structure based ellipticine (**1**) showed potential *in vitro* cytotoxicity (IC_{50} = 1.48 μM) against human glioma U87 MG cell line[19]. Carbazole structure based vinca alkaloid like vincristine (**2**) showed potential *in vitro* anticancer activity (IC_{50} = 1.317 μM) against U87 MG cell line[20]. Vincristine is delivered via intravenous infusion (IV) only and neuropathy side effects are two major disadvantages[12]. Mahanine (**3**), a pyranocarbazole alkaloid found potential *in vitro* cytotoxic effect (IC_{50} = 12-15 μM) against human glioma U87 MG cell line [21-22]. Carbazole 3-substituted sulfonamides derivative (**4**) linked to A ring part of combretastatin structure related to combretastatin (CA-4, **5**) structure showed potential *in vitro* anticancer activity (IC_{50} = 56 nM) against CEM leukemia cell line [23]. Combretastatin **(C**A-4, **5**) has a common trimethoxy benzene nucleus in their structures play an important role in biological activity [23,24]. Modified carbazole derivative (**6**) displayed excellent *in vitro* anticancer activity IC_{50} value 80 nM against glioma cell line [25]. Recently, our published research papers substituted biscarbazole derivatives[4] and substituted carbazole bearing thiosemicarbazide derivatives[26] respectively found significant *in vitro* anticancer activity against human glioma U87 MG cell line using MTT assay in 2020 & 2022 respectively. Alkylating agents like Procarbazine, Carmustine((1,3-bis(2-chloroethyl)-1-nitrosourea, BCNU**7**), Temozolomide (3-methyl-4-oxoimidazo[5,1-d][1,2,3,5]tetrazine-8-carboxamide, **8**) have played a major role in the chemotherapeutic treatment of GBM [4,5,27-28]. BCNU (**7**) displayed potential *in vitro* anticancer activity (IC_{50} = 18.24 μM) against U87 MG cell line [29-30]. BCNU can form interstrand crosslinks in DNA, which prevents DNA replication and DNA transcription. BCNU has major disadvantage short half-life around 20 minutes[4]. Most promising drug used in GBM treatment is TMZ (**8**), a prodrug approved by FDA in 1995 showed good *in vitro* anticancer activity (IC_{50} = 100 μM) against human glioma U87 MG cell line[31, 32]. Temozolomide is an imidazotetrazine derivative of dacarbazine alkylating drug [27-28, 33].

The majority of the known standard drugs alkylate the DNA in a non-specific manner, forming cross links within the DNA, and thus preventing the cell duplication which results in the anticancer activity.

To address the problems like non specificity, short half-life, toxicity associated with these clinical approved drugs, there is the option of attaching these ligands to known targeting molecules. The rational approach was the construction of carbazole based molecules behaves as minor groove binder or intercalator with DNA also coupled with a 2-chloro ethyl group with or without urea to act as a mono alkylating group [34]. Urea based anticancer agents extensively reported in review literature[35]. Carbazole scaffold also coupled to substituted piperazine pharmacophore and evaluated their anticancer activities against U87 MG glioma cell line. This has may increase specificity, with fewer side effects and more biological response is achievable using lower concentrations. To consider the potential biological activities of carbazole derivatives[36-38], we synthesized novel 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine derivatives and evaluated their anticancer activity against U87 MG glioma cell line using MTT assay.

1.2. Synthesis of 1, 4-dimethyl-9-*H*-carbazol-3-yl)methanamine and its derivatives (14-24)

In this work, the synthesis of 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine scaffold **13** was carried accoding to reported craxon and method[4, 38-39]. Intermidate **10**, **11**, **12** prepared according to our previous paper publihed and other research papers method [4, 38-39]. Briefly, the starting material indole **9**, 2,5-hexanedione in equimolar amount and catalytic amount of PTSA (para-toluene sulfonic acid) in solvent ethanol was reflux for 4h gave 1,4-dimethyl-9-H-carbazole ring after column or recrytallization method using petroleum ether (**10**). Vilsmeier-Haack formylation reaction on compound 1,4-dimethyl-9-H-carbazole (**10**) carried in the presence of N-methylformanilide and $POCl_3$ in 1,2 dicholobenzene at 80^0C for 3.5 h to obtaineded 1,4-dimethyl-9-*H*-carbazol-3-carbaldehyde **11**. Further, the reaction of the compound **11** with one equivalant of hydroxyl amine hydrochloride and few drops of water in ethanol solution strirred at rt for 4 h to gave 1,4-dimethyl-carbazol-3-oxime **12** as solid precipitate, which was filtered, washed with 10 ml ethanol and used without further purification. Reduction of the compound **12** carried with lithium aluminum hydride (LAH, 3equivalent) as reducing agent in tetrahydrofuran (THF) solvent, the reaction mixture was reflux for 6 h to give pure compound 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine scaffold **13** after column purification with 65 percent yield[40]. In series (A), the compounds (**14-17**) were prepared from reaction of compound **13** (0.05 mol), triethylamine (0.06 mol) in dichloromethane (DCM) solvent with constant stirring at 0–5°C for 5 minutes, gradually added acetic anhydride/chloroacetyl chloride/propionyl chloride/2-chloro ethyl isocyanate (0.06 mol) drop wise[41]. The reaction mixture stirred for 30 minutes to 12 h and the solvent was evaporated. The crude compounds (**14-17**) were purified by column chromatography in 70-80 % yield (**Scheme 1)**. In series B, the compounds (**18-19**) were prepared by refluxing 2-chloro-N-(1,4-dimethyl-9-H-carbazol-3-yl)methyl)acetamide **15**

(1.65 mmol, 0.5 g) in acetonitrile, added the appropriate methyl or ethyl piperazine (1.98 mmol) and dry K_2CO_3 (1.98 mmol, 0.3g) for 6 hour. The reaction mixture was cooled, filtered and the solvent was evaporated. Desired compounds (**18-19**) were purified by silica gel column chromatography in 65-70 % yield (**Scheme 1)** [42**]**. In series (**C**), the schiff bases of the 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine scaffold (**20-21**) were prepared via a condensation reaction of compound **13** with 4-bromo benzaldehyde/4-methoxy benzaldehyde in a molar ratio of 1:1 and sodium hydroxide in solvent DMF stirred room temperature for 36-48 h [246]. The solvent was evaporated to dryness and the crude product was purified by column chromatography in 10% ethyl acetate/petroleum ether to afford pure compound (**20-21**) in 40 % yield (**Scheme 1**). In series D, the compounds (**22-24**) were prepared by the reaction of compound **13** with stoichiometric amount of 4-bromo benzoic acid/4-methoxy benzoic acid/3,4,5 trimethoxy benzoic acid in DMF solvent added coupling reagent EDC. HCl N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride) and 1-hydroxyl benzotriazole (HOBT), DIPEA(Di-isopropyl ethylamine) stirred the reaction mixture for 12h to give the corresponding 4-bromo-1,4-dimethyl carbazole benzamide(**22)**, 4-methoxy 1,4-dimethyl carbazole benzamide (**23**) and 3,4,5-trimethoxy-1,4-dimethyl carbazole benzamide (**24**) compounds respectively after column purification in 40 % ethyl acetate/petroleum ether (**Scheme 1)**.

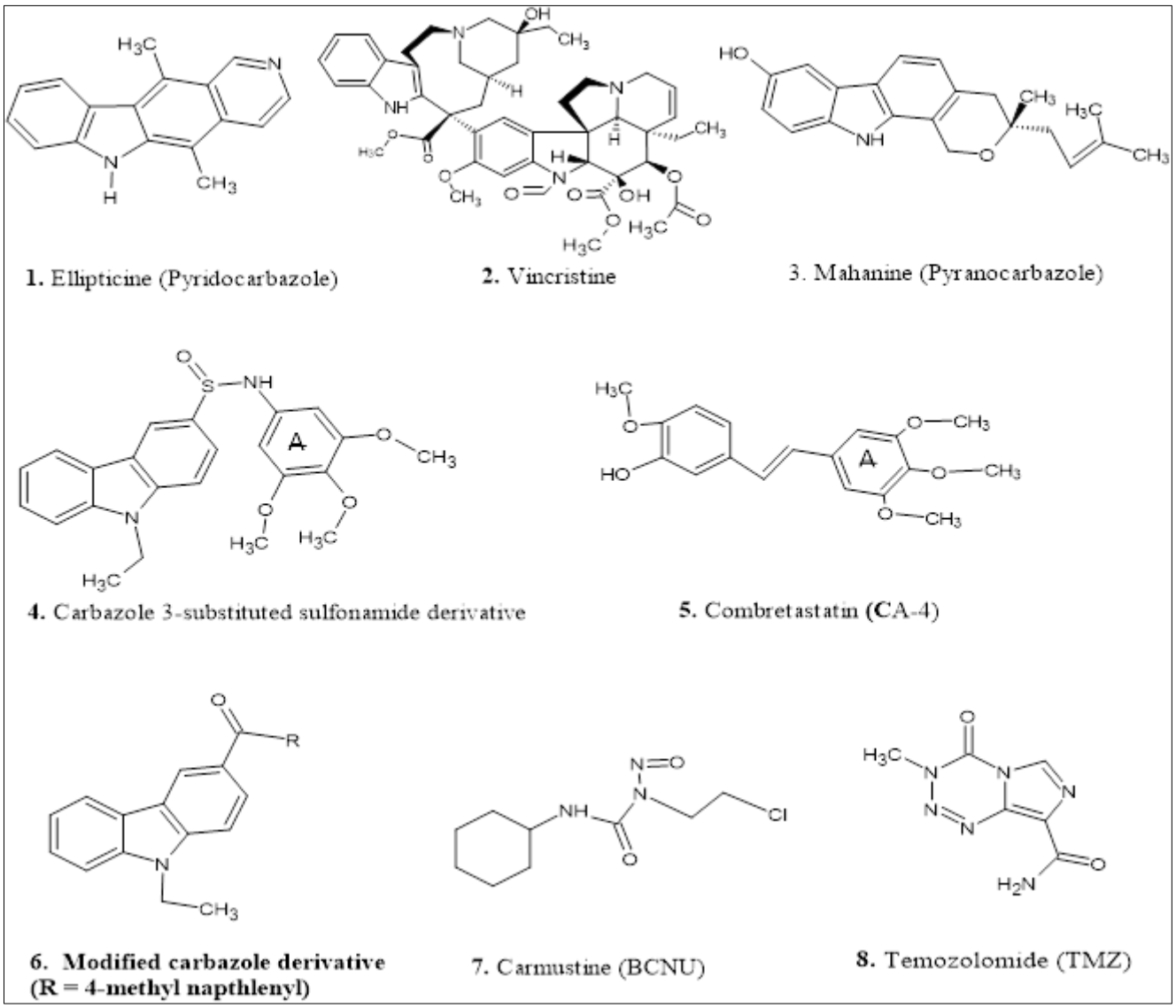
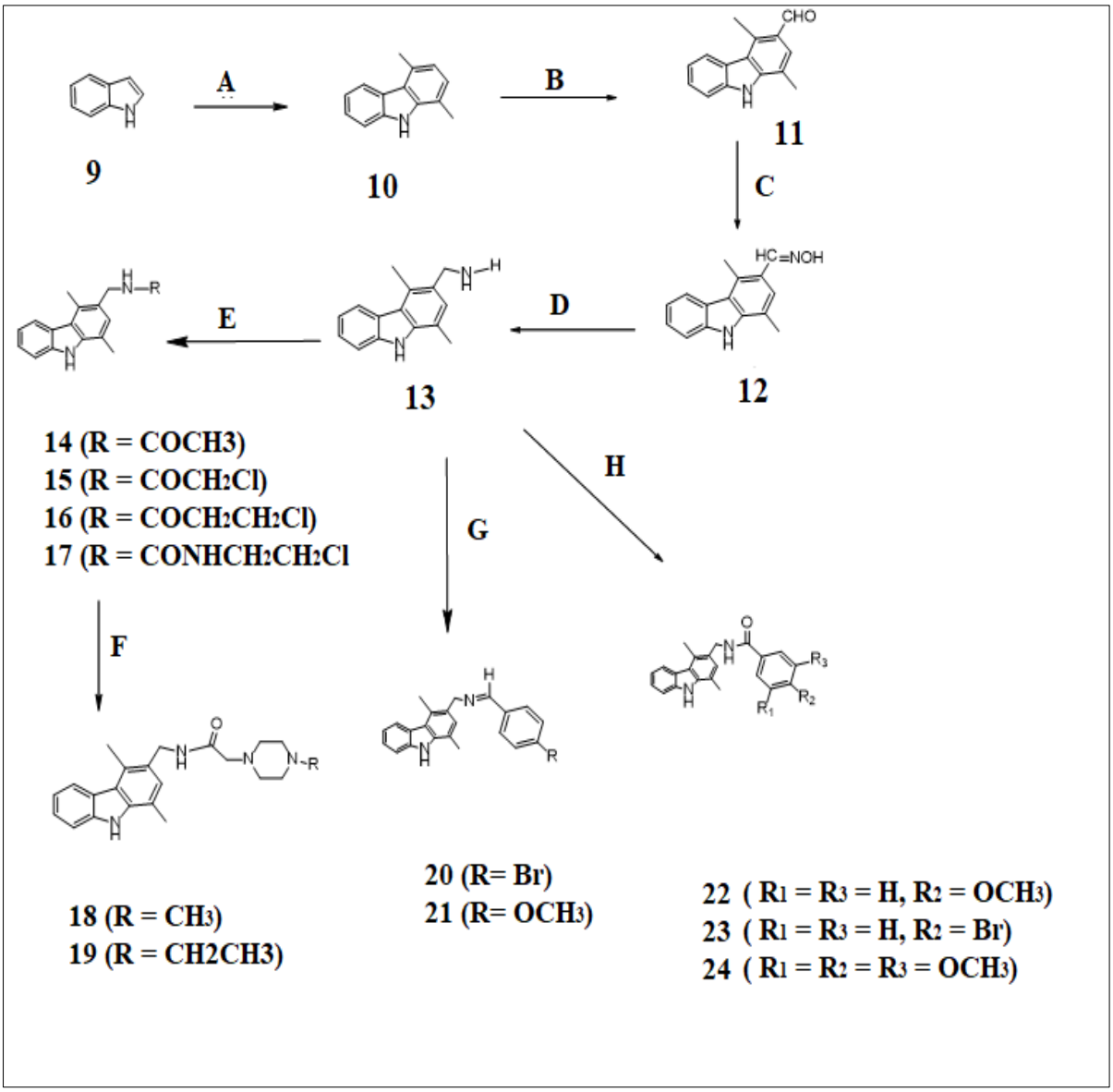


Figure 1 Structure of potential anticancer molecules like Ellipticine (**1**), Vincristine (**2**), Mahanine (**3**), Carbazole sulfonamides (**4**), Combretastatin (**5**), Modified Carbazole derivative (**6**), BCNU (**7**), TMZ (**8**)



Scheme 1 Reagents and conditions: A) 2,5 Hexanedione, para-toluene sulfonic acid, ethanol, reflux 4h B) N-methyl formanilide, $POCl_3$, 1,2-dichlorobenzene, heat at 80˚C, 3.5 h C) Hydroxylamine hydrochloride, H_2O, RT, 4h D) LAH, THF Solvent, reflux, 6 h E) Acetic anhydride or chloro acetyl chloride or propionyl chloride or 2-chloroethyl isocyanate, TEA, DCM, RT,1h-6h F) Compound 15, K_2CO_3, methyl or ethyl piperazine, ACN, reflux ,6 h G) NaOH, substituted aldehyde, RT, 36 h H) EDC, HOBT, DIPEA, substituted acid, RT,12 h.

2. Experimental section

2.1. Instruments used

All novel synthesized compounds prepared in our laboratory and well confirmed by melting point, NMR and HRMS (High resolution mass spectroscopy). Staring materials purchased from Spectrochem Pvt Ltd. (India), Sigma Aldrich, and Alfa Aesar. Proton ^1H NMR spectra were recorded on a Bruker Avance II and JEOL 400 MHz NMR spectrophotometer respectively. Mass (HRMS) of the compounds was taken by using a Micromass, Q-Tof micro (Water) spectrophotometer.

2.2. Cell lines and Culture Conditions

Human glioma U87 MG cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) with heat inactivated Fetal bovine serum (FBS) 10% (v/v), antibiotic and antimycotic solution. Cells were grown in a humidified incubator at 37^0 C supplemented with 5% CO_2 and 95% air during the night. The next day cells adhere to the culture matrix were treated

with or without compounds **13-24** for 24 h time phase[4, 43-44]. MTT assay of test compound 0-250 µM concentration were performed in triplicate.

2.3. Cell viability MTT assay

Treatment of cells (5×10^3 U87) with different concentrations (0-250 µM) of synthesized compound (**14-24)** for 24 h time period. Only, compound **13** concentration used for MTT assay from 0-500 µM to determine IC_{50} value. The IC_{50} value was calculated using the MTT assay formula in reported literature [4,43, 44].

2.4. General procedure for synthesis of 1,4-dimethyl-9-*H*-carbazol-3-yl methanamine (13)

Carbazole oxime compound **12** was prepared from earlier published method [4, 38]. A solution of the oxime **12** (0.00840 mol, 2g) prepared in our previous research paper [4] in tetrahydrofuran (50 ml) was heated at 50^0 C added drop wise to a stirred, boiling solution of lithium aluminum hydride (0.01068 mol,0.6 g) in tetrahydrofuran solvent (20 ml) in 20 minutes at such a rate that gentle refluxing was maintained. Reflux the reaction mixture for 4-6 h. Stop the reaction and cool down. Added cold water cautiously (20 ml) in reaction mixture solution. The reaction mixture was evaporated in vacuum pump and further purified by column chromatography using silica gel with 15 percent ethyl acetate/petroleum ether mixture to get the pure compound **13** white pure product.

(1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine(13): Yield: 67 %. Pale red solid; mp:221ºC. ^{1}H NMR (DMSO): δ 8.15 (d,1H) ,7.67 (s,1NH),7.3(m,2H), 7.12 (m, 1H), 6.68(s,1H),2.89(s,CH_2),2.59(s,CH_3),2.46(s,CH_3),HRMS (ESI-Q-TOF): $C_{15}H_{16}N_2$ $[M + H]^+$ calcd m/z ,224.1317, found M/Z 225.1390

2.5. General procedure for synthesis of (1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine derivatives (14-17)

Compound **13** (0.89 mmol,0.2 g) and triethylamine (0.89 mmol ,0.1 ml) in DCM with a constant stirring at 0–5°C for 5 minutes, added acetic anhydride (0.89 mmol ,0.1 ml) or chloroacetyl chloride (0.89 mmol ,0.12 ml) or propionyl chloride (0.89 mmol ,0.12 ml) or 2-chloro ethyl isocyante(0.89 mmol ,0.12 ml) was added drop wise gradually to this solution. The reaction mixture stirred rt for 1h-12 h. After the solvent was evaporated to dryness and pure target compounds (**14-17**) were obtained by 10-50% ethyl acetate/petroleum ether mixture using silica gel column chromatography in 80-90 % yield.

N((1,4-dimethyl-9-*H*-carbazol-3-yl)methyl)acetamide(14) Yield: 90%. White solid; mp:205 ºC. ^{1}H NMR (CDCl3): δ 8.14(d,1H),7.67(s,1NH),7.46(s,NH),7.42(1H,s),7.20(2H,d),6.9(s,1H),3.2(s,CH_2),2.63(s,CH_3),2.48(s,CH_3),1.73(s,CH_3). HRMS(ESI-Q-TOF):$C_{17}H_{18}N_2O$ $[M+H]^+$ calcd m/z , 266.1427, found M/Z 267.1504.

2-chloro-N((1,4-dimethyl-9-*H*-carbazol-3-yl)methyl)acetamide(15): Yield: 80%. White solid; mp:270 ºC. NMR (DMSO): δ 11.39(s,1NH), 8.12(d,1H), 7.52(d,1H), 7.38(s,1NH), 7.13(m,2H), 3.65(q,2H), 3.13(s,CH_2), 2.51(s,CH_3), 2.49(s,CH_3). HRMS (ESI-Q-TOF):$C_{17}H_{17}ClN_2O$ $[M+H]^+$ calcd m/z ,300.103, found m/z 301.1103.

3-chloro-N((1,4-dimethyl-9*H*-carbazol-3-yl)methyl)propanamide(16): Yield: 85%. White solid; mp:251ºC.^{1}HNMR (CDCl3): δ, 8.15(d,1H), 7.67(s,1NH), 7.32(s,1H), 7.13(m,1H), 6.68(s,1H). 3.65(t,2H), 3.43(t, 2H), 3.12(s,CH_2),2.50(s,CH_3). HRMS(ESI-Q-TOF):$C_{18}H_{19}ClN_2O$ $[M+H]^+$ calcd m/z 314.1193, found M/Z 315.1267.

2.6. General procedure for synthesis of (1,4-dimethyl-9-*H*-carbazol-3-yl) methanamine –piperazine substituted derivatives (18-19)

Starting material: 2-chloro-N-(1,4-dimethyl-9-*H*-carbazol-3-yl)methyl)acetamide **15** (1.65 mmol, 0.5 g), the appropriate methyl or ethyl piperazine(1.98 mmol) and dry K_2CO_3 (1.98 mmol, 0.3g) added in acetonitrile was refluxed for 6 hours. The cooled mixture was filtered, evaporated and further purified by 10 % methanol/ chloroform via column chromatography to gave pure target compound 12-13 in 60-70 % yield.

N((1,4-dimethyl-9-H-carbazol-3-yl)methyl)-2-(4-methylpiperazin-1-yl)acetamide (18): Yield: 65 %. White solid; mp:310ºC. ^{1}H NMR (DMSO) δ:11.40(s,1NH),8.15(d,1H),7.59(d,1H),7.40(m,1H),7.30(m,1H),7.15(s,1H), 3.10(s,CH_2), 2.46(s,CH_3), 2.58(q, CH_2), 2.32(m,8-CH_2)0.936(t,CH_3). HRMS (ESI-Q-TOF):.$C_{22}H_{28}N_4O$ $[M+H]^+$calcd m/z 364.225 ,found M/Z 365.2322.

2.7. General procedure for synthesis of amides Series D compounds (22-24)

They were prepared the reaction of compound **13** with stoichiometric amount of 4-bromo benzoic acid or 4-methoxy benzoic acid or 3,4,5 trimethoxy benzoic acid in DMF solvent added coupling reagent EDC. HCl (1-3Dimethylaminopropyl)-3-ethylcarbodiimide) and 1-hydroxyl benzotriazole (HOBT), DIPEA were stirred at rt for 12 h gave the corresponding 4-bromo-1,4 dimethyl carbazole benzamide (**22**), 4-methoxy 1,4 dimethyl carbazole benzamide (**23**) and 3,4,5 trimethoxy 1,4 dimethyl carbazole benzamide (**24**) compounds respectively. The cooled mixture was filtered, evaporated and further purified by 10 % methanol/ chloroform via column chromatography to give pure target compound 14-16 in 70-75 % yield

N((1,4-dimethyl-9-H-Carbazol-3-yl)methyl)-4-bromobenzamide(22): Yield: 76 %. White solid; mp: 315ºC. 1H NMR (CDCl3): δ 8.30 (s, NH),8.02 (d,1H),7.38 (m, 2H), 7.23(m,3H),6.87(s,1H), 6.67 (d ,2H), 3.87 (s,CH2), 2.59(s,CH3), 2.46 (s,CH3), HRMS (ESI-Q-TOF):. $C_{22}H_{19}BrN_2O$ $[M + H]^+$ calcd m/z, 390.07 found M/Z 391.2832

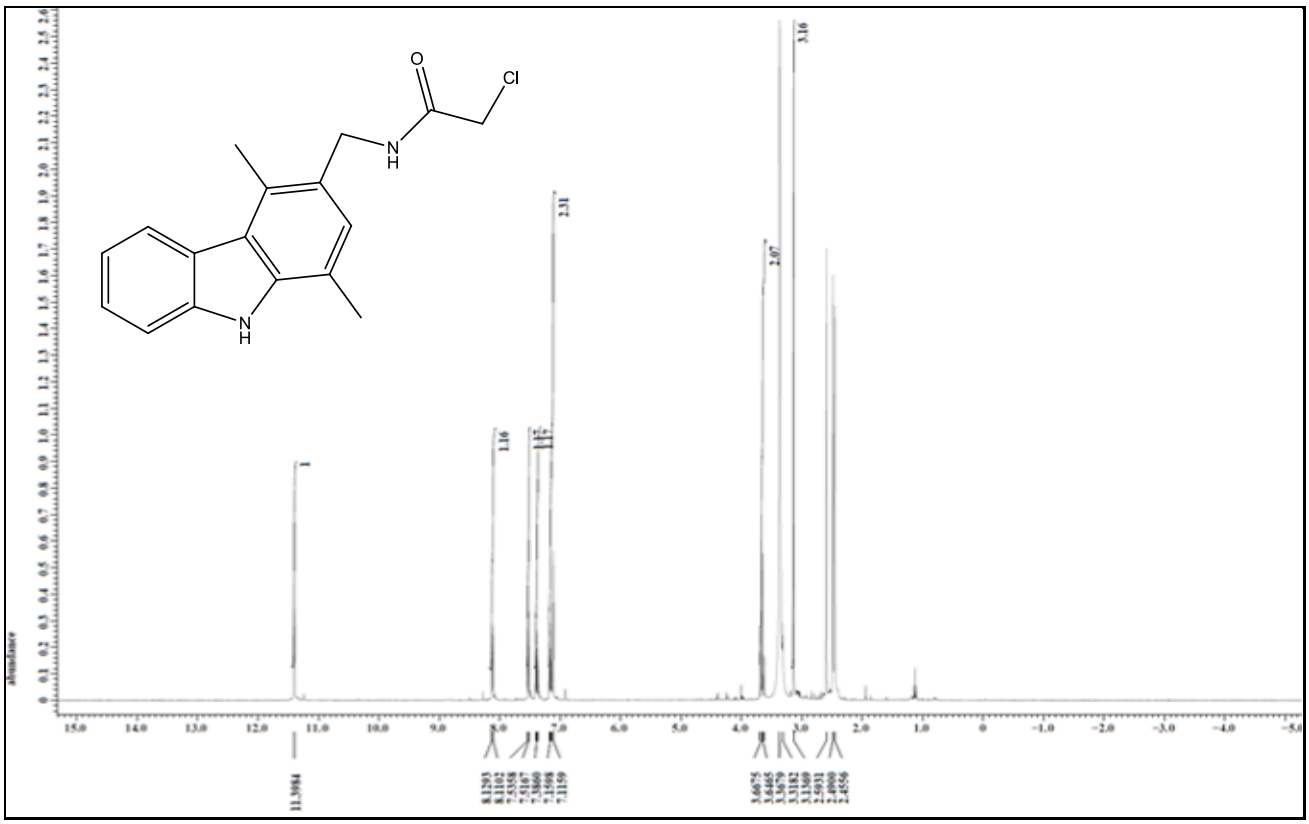


Figure 2 Proton NMR spectra of 2-chloro-N((1,4-dimethyl-9-*H*-carbazol-3-yl)methyl) acetamide (15)

Table 1 *In vitro* anticancer activity of 1, 4-dimethyl-9-H-carbazol-3-yl) methanamine and its derivatives (13-24) against U87 MG cell line using MTT assay

S.No.	Linker(R)	IC_{50}(µM)
13	H	446
14	$COCH_3$	>250
15	$COCH_2Cl$	18.50
16	$COCH_2CH_2Cl$	47
17	$CONHCH_2CH_2Cl$	75
18	Piperazine-1 (R = CH_3)	>250
19	Piperazine-2 (R = CH_2CH_3)	>250

20	Schiff base 1 (R = Br)	160
21	Schiff base 2 (R = OCH_3)	175
22	Amide-1 (R_1 = R_3= H, R_2 = OCH_3)	>250
23	Amide-1 (R_1 = R_3= H, R_2 = Br)	>250
24	Amide-1 (R_1 = R_3= R_3 = OCH_3)	180
TMZ	----------	100
(BCNU)	----------	18.24

Compound 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine scaffold **13** showed poor IC_{50} value 446 μM against human glioma U87 cell line. However, compound **13** have with alkyl amine were substituted with Chloro acetyl group (**15**), ethyl chloro acetyl group (**16**) and urea with 2-chloro ethyl group (**17**) showed potential *in vitro* cytotoxicity (IC_{50}) values 18.50 μM, 47 μM and 75 μM respectively. Compound N((1,4-dimethyl-9-*H*-carbazol-3-yl)methyl)acetamide (14) showed no IC_{50} value up to 250 μM. In series A three compounds (**15-17**) showed better *in vitro* cytotoxicity (IC_{50}) values 18.50 μM, 47 μM and 75 μM against U87 MG cell line compared to clinically approved alkylating drug TMZ (IC_{50}= 100 μM). In series A, compound 2-chloro-N((1,4-dimethyl-9-*H*-carbazol-3-yl)methyl)acetamide (15) showed significant *in vitro* cytotoxicity (IC_{50} = 18.50 μM) comparable to standard drug BCNU (IC_{50} =18.24 μM) against U87 MG cell line. Compound **15** and **16** showed better *in vitro* cytotoxicity(IC_{50}) value than compound **17** showed that urea with 2-chloro ethyl group is not essential for potent in vitro anticancer activity (**Table-1**). Carbazole linked with substituted piperazine also show loss of *in vitro* anticancer activity against U87MG cell line (>200 μM) (**Table-1**). In series B compound **18** and **19** also found no *in vitro* cytotoxicity (IC_{50}) value up to 250 μM respectively against U87 cell line. In series C Schiff bases of compound **20** and **21** showed poor *in vitro* cytotoxicity (IC_{50}) values 160 μM and 175 μM against U87 cell line. In series D two compounds **22** and **23** showed no in vitro cytotoxicity (IC_{50}) value up to 250 μM concentration against human glioma U87 cell line. In series, compound **15** showed best *in vitro* cytotoxicity profile (IC_{50} = 18.50 μM) better than Temozolomide (IC_{50} = 100 μM) and equipotent to carmustine (IC_{50} = 18.24 μM) respectively.

3. Conclusion

In summary, we have designed and synthesized 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine and its derivatives **(14-24**). All target compounds (**14-24**) were well characterized by NMR and HRMS spectroscopy techniques. All final compounds (**14-24**) were examined for *in vitro* anticancer activities (IC_{50}) against U87 MG human glioma cell line using MTT assay. In series compound **15** found better *in vitro* cytotoxicity(IC_{50} = 18.50 μM) compare to standard drug TMZ(IC_{50} = 100 μM) respectively against human glioma U87 MG cell line. Further, two compounds based on carbazole structure (**16-17**) also found excellent *in vitro* anticancer activity (IC_{50}) values 47 μM and 75 μM respectively against human glioma U87MG cell line. In series, some 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine derivatives did not show IC50 value up to 250 μM against tested human glioma U87 MG cell line. Carbazole linked with piperazine pharmacophore found no *in vitro* anticancer activity against U87MG cell line in our tested compound concentration (0-250 μM) using MTT assay. Carbazole Schiff based derivatives also showed poor anticancer profile against U87 MG cell line. The study of novel 1,4-dimethyl-9-H-carbazole derivatives found potential *in vitro* anticancer activities against U87MG human glioma cell line. This research may be helpful to design and development of novel anti-glioma agents based on 1,4-dimethyl-9-*H*-carbazol-3-yl)methanamine scaffold.

Compliance with ethical standards

Acknowledgments

Dr. Pratibha Metha Luthra is very thankful to DST, India (SR/SO/HS-40/2004) for project grant. Dr. Nitin Kumar (CSIR) (9/45(1337)2014-EMR-1) and Dr Neetika Lal, are thankful to Council of Scientific and Industrial Research (CSIR) New Delhi, India for fellowship. Dr. Vishal Nemaysh is thankful to U.G.C. for financial support. We are thankful to University Instrumentation Facility (USIC) for providing ^{1}HNMR, and HRMS data through the central instrumental facilities.

Disclosure of conflict of interest

The authors confirm that this article content has no conflicts of interest.

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