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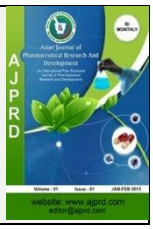

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Review Article

A Review on Biological Activity of Heterocyclic Nucleus Carbazole

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ABSTRACT

In this article we aimed to review existing literature and relevant websites regarding to heterocyclic nucleus such as carbazole and discussed about its biological activity. Carbazole contain most of the biological activities such as anti-inflammatory, antihypertensive, antianginal, antiarrhythmic etc. In this article we also discussed about the various carbazole containing drugs and there uses, IUPAC name and synthesis of carbazole nucleus.

Key words: Carbazole, antiarrhythmic, antianginal

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INTRODUCTION

The history of heterocyclic chemistry began in the 1800s, in step with the development of organic chemistry. Some noteworthy developments were: *Brugnatelli* isolated alloxan from uric acid (1818), *Dobereiner* produced furfural (a furan) by treating starch with sulphuric acid (1832), *Runge* obtained pyrrole ("fiery oil") by dry distillation of bones (1834), *Friedlander* synthesized indigo dye, allowing synthetic chemistry to displace a large agricultural industry (1906), *Treibs* isolated chlorophyl derivatives from crude oil, explaining the biological origin of petroleum (1936), *Chargaff's* rules were described, highlighting the role of heterocyclic compounds (purines and pyrimidines) in the genetic code (1951)[1].

Heterocyclic chemistry has its origin in organic synthesis, natural products chemistry and medicinal chemistry. Indeed most any heterocyclic chemist will also consider themselves organic chemists and many will consider themselves to be natural products chemists and medicinal chemists as well.This relationship between disciplines arises because heterocyclic molecules are fundamental building blocks of biological systems. In addition to its importance to biology, heterocyclic chemistry has seen intense study in diverse areas such as dyes, photosensitizers, coordination compounds, polymeric materials and many other fields[2].

Heterocyclic compounds

A heterocyclic compound is defined as any organic compound where their molecules are characterized by rings containing at least one atom other than carbon. These compounds are structurally similar to cyclic organic hydrocarbons, but their properties can vary widely from those of their hydrocarbon counterparts and are largely governed by the identity, location and number of heteroatoms present in the molecule. It is this rich diversity of physical and biological properties that has led to intense study of heterocyclic compounds. It follows then that heterocyclic chemistry is the study of all aspects of heterocyclic compounds[3]

Heterocyclic systems are ring compounds containing atoms of at least two different elements as ring members. Organic heterocyclic systems contain one or more "foreign" elements such as oxygen, sulphur or nitrogen in addition to

carbon; atoms of such elements conceptually replacing carbon in a ring system have long been called hetero atoms.

In recent years, however, the meaning of the term heteroatom has been broadened to include atoms other than carbon occurring in chains as well as in rings. The general method of naming organic ring and chain systems based on the hetero atom concept is known as replacement nomenclature[4]

Compounds classified as heterocyclic probably constitute the largest and most varied family of organic compounds. After all, every carbocyclic compound, regardless of structure and functionality, may in principle be converted into a collection of heterocyclic analogues by replacing one or more of the ring carbon atoms with a different element. Even if we restrict our consideration to oxygen, nitrogen and sulphur (the most common heterocyclic elements), the permutations and combinations of such a replacement are numerous

CARBAZOLE

Abbreviation:	CARBAZOL
IUPAC name:	9*H*-Carbazole
Synonyms:	• 9-Azafluorene • Dibenzo[b,d]pyrrole • Diphenylenimide • Diphenylenimine

Carbazole is an aromatic heterocyclic organic compound. It has a tricyclic structure, consisting of two six-membered benzene ring fused on either side of a five-membered nitrogen-containing ring (Pyrrole).

The structure of compound is based on the indole structure but in which a second benzene ring is fused onto the five-membered ring at the 2-3 position of indole (equivalent to the 4a-9a double bond in carbazole)[6].

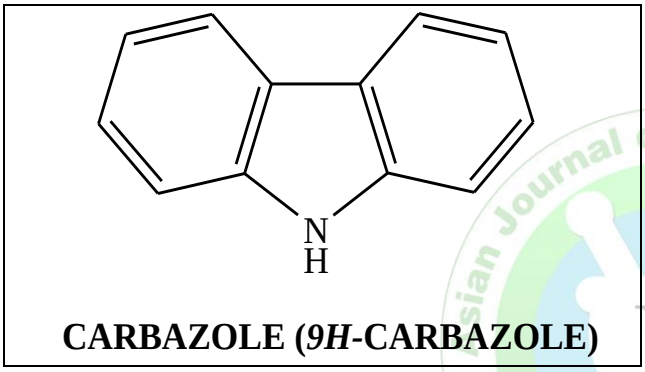


Figure: 1 Carbazole (9H-Carbazole)

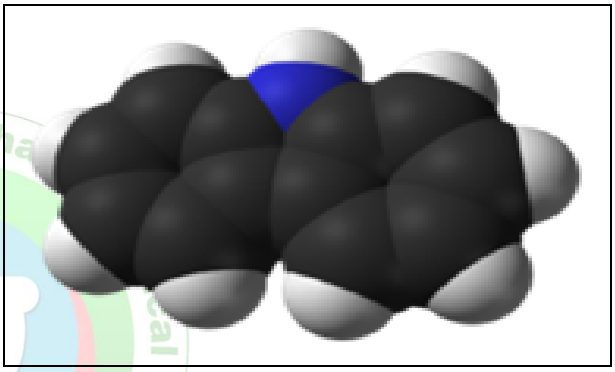


Figure: 2 Space filling model of carbazole

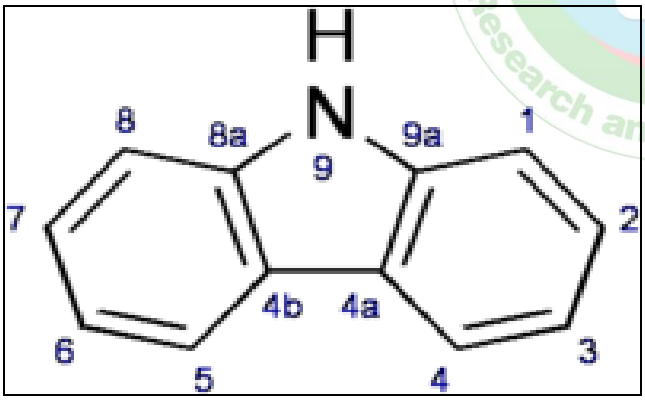


Figure: 3 Structure with numbering

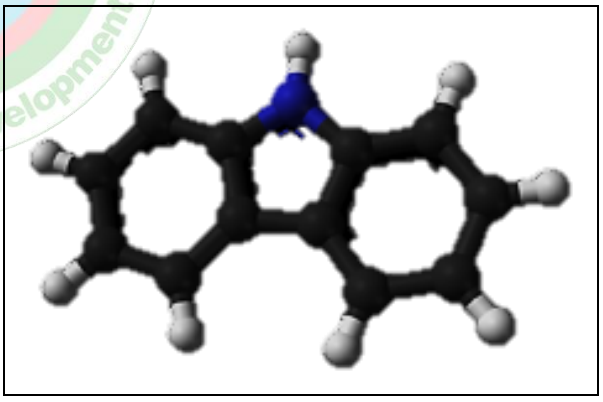


Figure: 4 Ball and stick model

Carbazole and its derivatives are an important type of nitrogen containing aromatic heterocyclic compounds, possess desirable electronic and charge-transport properties, as well as large π-conjugated system, and the various functional groups are easily introduced into the structurally rigid carbazolyl ring. These characteristics result in the extensive potential applications of carbazole based derivatives in the field of chemistry (photoelectrical materials, dyes, supramolecular recognition etc.) and medicinal chemistry (antitumor, antimicrobial, anticonvulsant, antihistaminic, anti-oxidative, anti-inflammatory, anti-diabetic, psychotropic agents, etc.).Carbazole alkaloids constitute an important class of naturally occurring heterocycles. A rough division of the carbazole alkaloids into three groups can be made. By far the largest group comprises alkaloids isolated from the Rutaceaefamily (=the Citrus family). The second group contains alkaloids of the hyellazole / carbazomycin, and the third group comprises of alkaloids that does not fall into the above two categories.

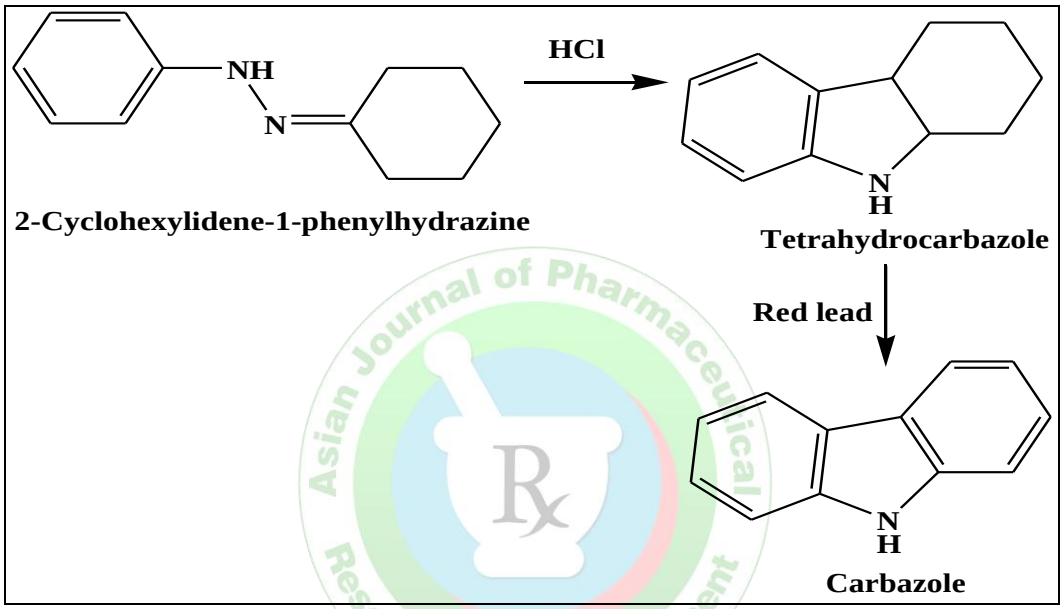
Carbazole alkaloids are of significant synthetic interest due to their range of biological activities. Carbazole rings are

present in a variety of naturally occurring medicinally active substances[7]

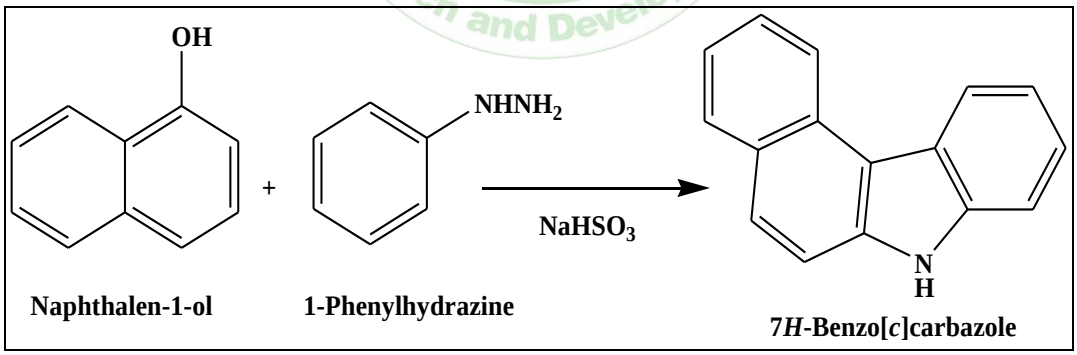
For example, the carbazomycins are an unprecedented class of antibiotics with a carbazole framework. Carbazomycins A and B inhibit the growth of Phytopathogenic fungi and have antibacterial and anti-yeast activities.Many derivatives of the naturally occurring alkaloids elipticine and 9-methoxyelipticine which contain carbazole ring in their structure have been developed and tested for their anticancer activity. Carbazole is one of the most predominant tricyclic aromatic *N*-heterocyclic compounds in coal tar creosote and crude oil. It is used as a chemical raw material for the production of dyes, medicines, and plastics. By the virtue of their widespread occurrence in both important natural products (e.g. Alkaloids) and unnatural synthetic materials, as well as the broad spectrum of biological activity associated with these compounds, carbazole derivatives have received considerable attention in the literature, particularly in terms of their synthetic methodology.It is well-known that azole moieties such as oxadiazole, thiadiazole, imidazole, triazole nucleus as important pharmacophore appear extensively in various types of pharmaceutical agents, widely implicate in biochemical processes and display diversity of pharmacological activities[8]

SYNTHESIS OF CARBAZOLE NUCLEUS AND DERIVATIVES

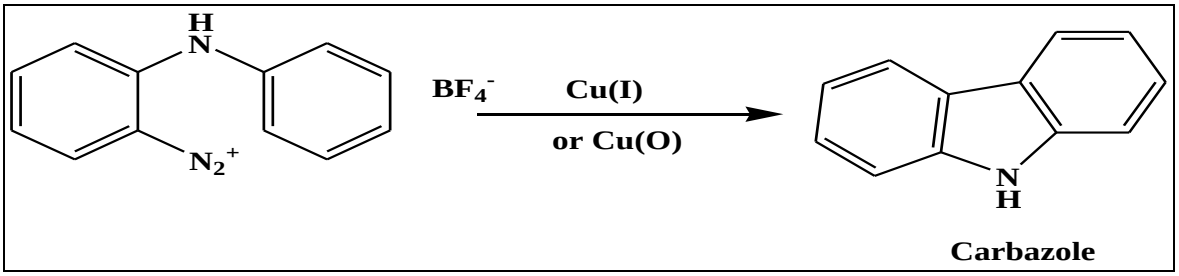
A. Borsche-Drechsel Cyclization



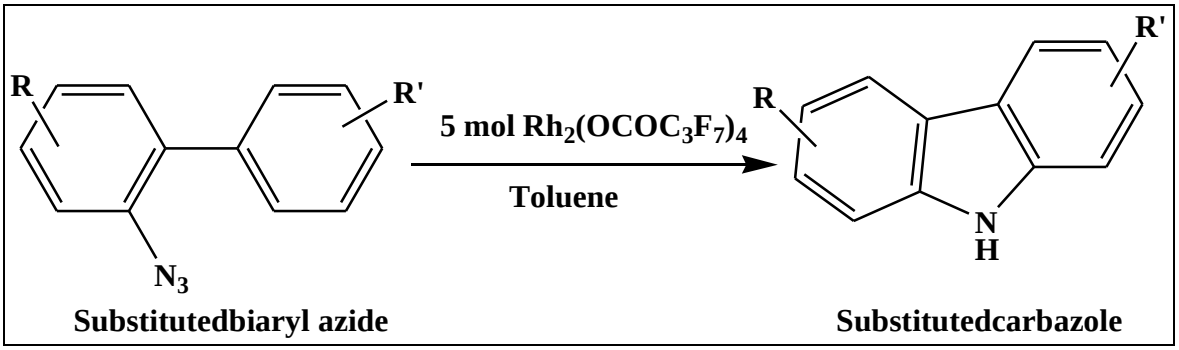
B. BuchererCarbazole Synthesis



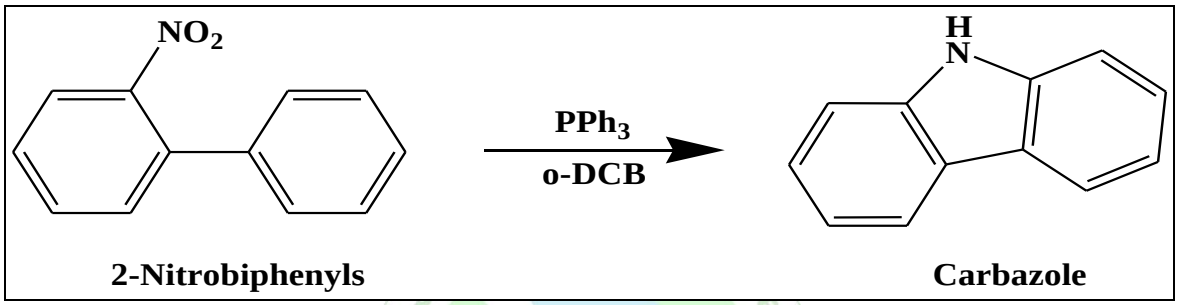
C. Pschorr Reaction



D. Various carbazoles can be synthesized from substituted biarylazides at 60°C using $Rh_2(OCOC_3F_7)_4$ or $Rh_2(OCOC_7H_{15})_4$ as catalysts[9]



E. Synthesis of Carbazole from cyclization of 2-nitrobiphenyls.



1.2 Marketed Drugs Containing Carbazole Moiety

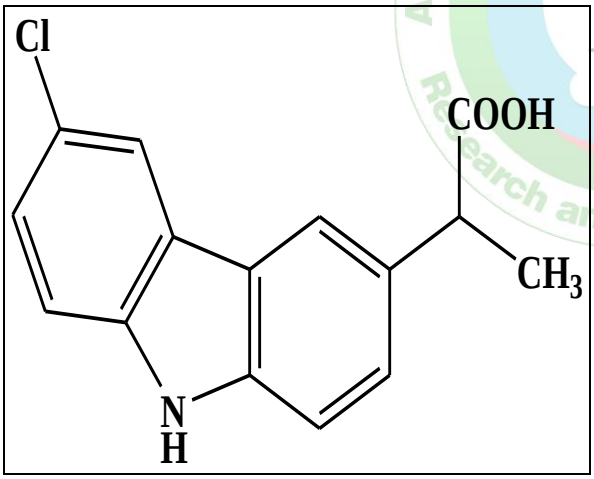


Figure: 5 Carprofen

IUPAC name: 6-Chloro-α-methyl-9*H*-carbazole-2-acetic acid.

Category: Anti-inflammatory

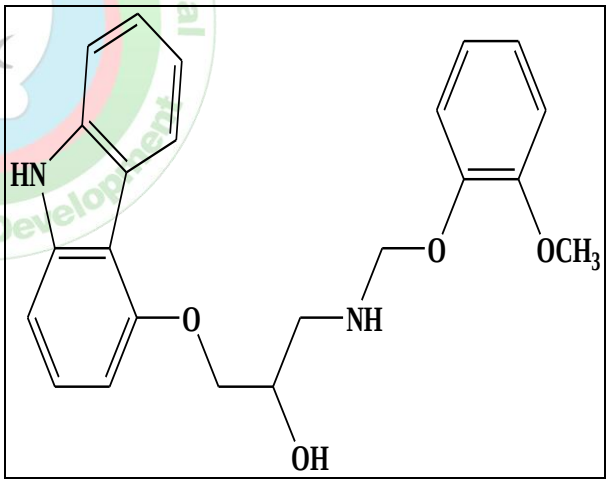


Figure: 6 Carvedilol

IUPAC name: 1-(9*H*-Carbazole-4-yloxy)-3-[{2-(2-methoxy-phenoxy) ethyl]-2-propanol.

Category: Antihypertensive

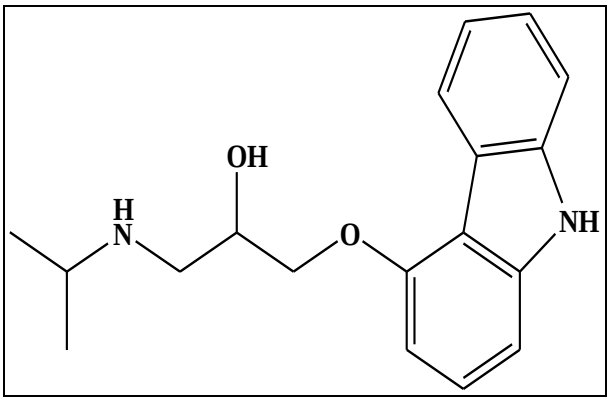


Figure: 7 Carbazolol

IUPAC name: 1-(9*H*-Carbazol-4-yloxy)-3-[(1-methyl-ethyl)amino]-2-propanol.

Category: Antihypertensive, Antianginal, Antiarrhythmic

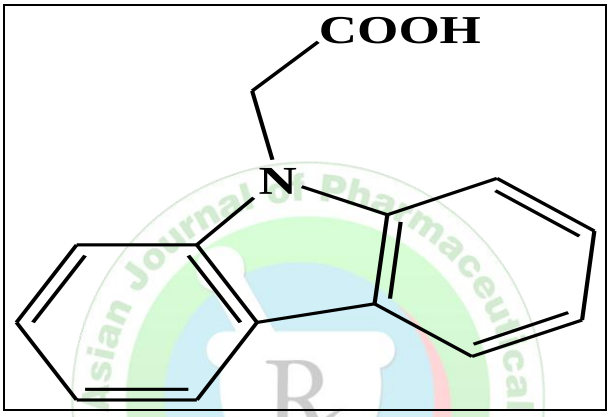


Figure: 8 Carbazoleacetic acid

IUPAC name: Carbazyl-*N*-acetic acid

Category: In the detection of nitrates

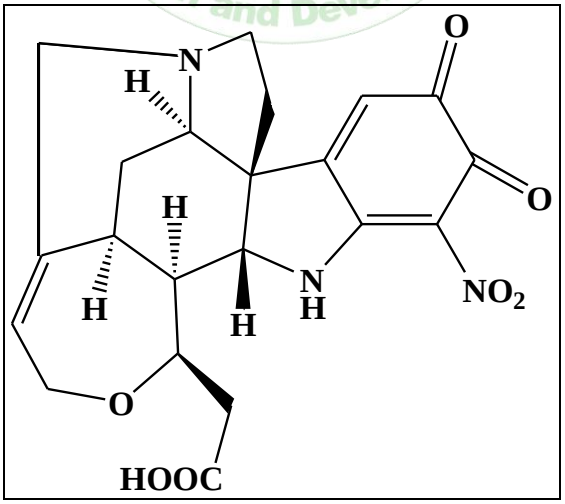


Figure: 9 Cacotheline

IUPAC Name: 2,3-Dihydro-4-nitro-2,3-dioxo-9,10-secostrychnidin-10-oic-acid

Category: Muscle relaxant[10]

REVIEW OF LITERATURE

Anti-microbial activity

Salih N. et al. (2016) synthesized a series of 9H-carbazole derivatives. The synthesized compounds were tested for in vitro antibacterial activity against gram positive bacteria [*Staphylococcus aureus* (ATCC 6538), *Bacillus subtilis* (NRRL B-14819) and *Micrococcus luteus* (ATCC 21881)] and gram negative bacteria [*Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa*(ATCC 27853)and *Klebsiella pneumonia*(clinical isolate)] by disk diffusion method by using Ampicillin trihydrate as standard drug. Compounds were also evaluated for in-vitro anti-fungal activity against fungi (*Candida albicans*, *Candida tropicalis*and *Candida krusei)* and moulds (*Aspergillusniger*, *Aspergillusfumigatus* and *Tricophytonrubrum)* by the serial plate dilution method using Clotrimazole and Miconazole as standard drugs. The result showed that Compound **12a** and **12b** has maximum antimicrobial activity[11].

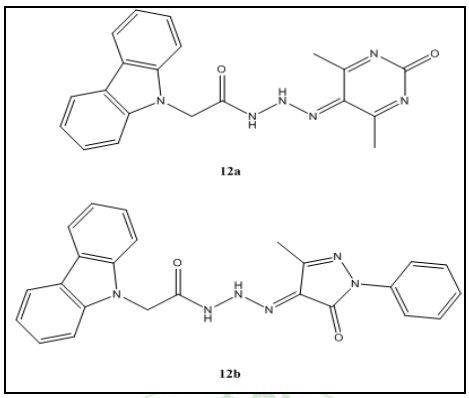


Figure: 10 Anti-microbial activity

Ahmad H. Abdullah et al. (2016) synthesized a selected set of *N*1-(4-chloro-9-ethylcarbazol-yl) amidrazones by reacting the respective hydrazonoyl chloride derived from 3-amino-9-ethylcarbazole, with an appropriate *sec*cyclicamine in ethanol in the presence of triethylamine .The compounds were evaluated for in-vitro antibacterial activity against Gram-positive [*S. aureus* (ATCC 25923), *S. aureus* (MRSA), *B. cereus* (ATCC 14579), *C. xerosis* (ATTCC 00000)] , Gram-negative bacteria [*Salmonella typhimurium* (ATCC 14028), *Klebsiellapneumoniae* (ATCC 700603),and *K. pneumonia* and *Shigellasonnei* (ATCC 9290)],and fungus [*Candida albicans]* by standard broth dilution assay by using gentamycin as standard drug. The result showed that the compounds **13a**and **13b** exhibit the highest activity against MRSA and *B. cereus*, respectively[12].

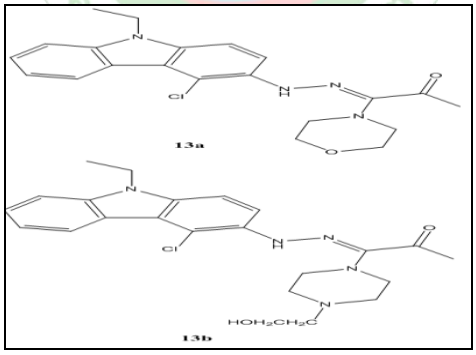


Figure: 11 Anti-cancer activities (compounds 13a and 13b)

L. V. Éktova et al.(2016) synthesized a indole [2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,6-dione. the synthesized compound were evaluated for in-vitro anticancer activity against the different cell lines i.e. Leukemia (K-562, MOLT-4), Non-small cell lung cancer (NCI-H322M, NCI-H522), CNS tumors (SF-539, SNB-75), Melanoma (M14 ,SK-MEL-2), Ovarian tumors (OVCAR-4, SK-OV-3), Renal tumors (A498,SN12C), Breast tumors (MCF-7, HS 578T), Colon tumors (HCT-116, COLO205) by using the standard MTT test using the MTT reagent 2,4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium bromide.

The result shows the all compounds exhibit the high level of anticancer activity (IC_{50}= 10 6 – 108 M)[13]*Pramod V. Chavanet al.*(2019) synthesized a series of spirochromenocarbazole tethered 1,2,3-triazoles derivatives by one-pot, five component condensation reaction. The synthesized compounds tested for in-vitro anticancer activity against a panel of six human cancer cells namely MCF-7 and MDA-MB-231 (Breast Carcinoma), HeLa (Cervical Carcinoma), PANC-1 (Pancreas Carcinoma), A-549 (Lung Carcinoma) and THP-1 (acute monocytic leukemia) by MIT assay by using standard drug Paclitaxel and Doxorubicin. The result shows that compounds, **6f, 6k, 6g, 6s** and **6u** showed excellent activity towards MCF-7, MDAMB - 231 and HeLa cancer cell lines. The compound 6j were shows the good activity for all three cancer cell lines[14].

Peng-Hui Li et al. (2018) synthesized a series of carbazole derivatives containing chalcone analogs (CDCAs).the compounds were evaluated for in-vitro antiprolifrative activity against four human cancer cell lines, including HeLa (human cervical cancer cell line), HL-60 (human acute leukemia cell line), A549 (adenocarcinomic human alveolar basal epithelial cancer cell line), and PC-3 (human prostate cancer cell line), by using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) assay by using stanadrad drug Etoposide. The result shows that Compound **14a** showed the most potent Topo II inhibitory activity[15].

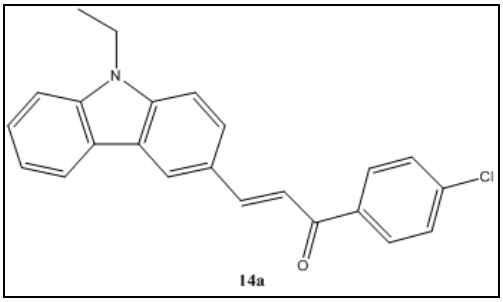


Figure: 12 Compound **14a**

Gang Li et al. (2019) synthesized a methylene-bridged bis-carbazole. The compound were evaluated for in-vitro anticancer activity against four human tumor cell lines (human breast cancer cell), HepG2 (human liver carcinoma cell), HT29 (human colon cancer cell) and A375 (human malignant melanoma cell) by MTT assay by using standard drugs 5-Fluorouracil Doxorubicin Paclitaxel. The result shows that's compound **15a**exhibited the best anti-proliferative activities against HT-29, HepG2, A375 as well as MCF-7 cell due possibly to its selective G4-DNA binding nature[16].

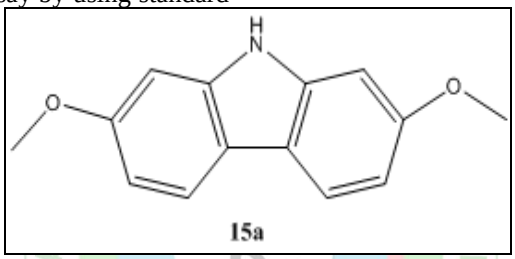


Figure: 13 compound **15a**

KarunanidhiMurali et al. (2017) synthesized a 2-amino-4-(3'-bromo- 4'-methoxyphenyl)-8-chloro-11*H*-pyrimido [4,5-*a*]carbazole. The compounds were evaluated for in-vitro antitumoractivities against two different cancer cell lines were utilized: MCF-7 (breast cancer) and A-549 (lung cancer) by MTT assay by using standard drug Cisplatin (IC_{50}-18±1.5).The result shows that Compound**16a** exhibited significant activity against MCF-7[17].

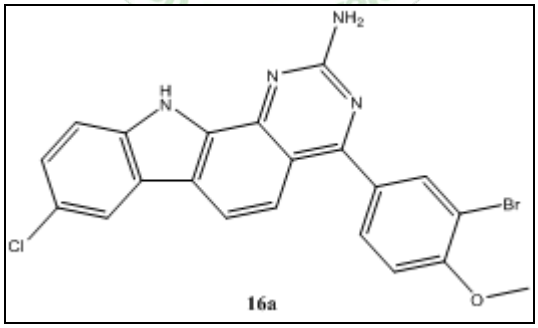


Figure: 14 Compound**16a**

KarunanidhiMurali et al.(2018) synthesized a dispirooxindole-pyrrolocarbazole hybrids *via* 1,3- dipolar cycloaddition reactions. The compound were tested for in-vitro cytotoxicity activity against two human cancer cell lines, MCF-7 breast cancer and A-549 lung cancer by MTT assay by using standard drug Cisplatin.The result shows that compounds **7e, 7f**and **7g**having thiophene moiety showed potentanti-proliferative activity[18].

Takashi Nishiyama etal. (2016) synthesized a carbazole-1,4-quinones derivatives. The compound were evaluated for in-vitro anti-proliferative activity against HCT-116 and HL-60 cell lines by MTT assay by using camptothecin as standard drug.The result shows monosubstituted derivatives were possess good anti-proliferative activity[19]. *PerumalSathiyachandran etal*. (2018) synthesized a pyrrolo[2,3-*a*]carbazoles: 7-Chloro-2-oxo-3a-(2'-oxo-2',3'-dihydro-1'*H*-indol-3'-yl)-2,3,3a,4,5,10-hexahydro-pyrrolo[3,2-*a*]carbazole-1-carbonitrile derivative .the compound were evaluated for in-vitro anticancer activity against colon cancer cell lines (HCT-15 cells) by MTT assay for 24 hrs. by using Cisplatin as standard drug.The result shows that Compound **17a** showed better anticancer activity[20].

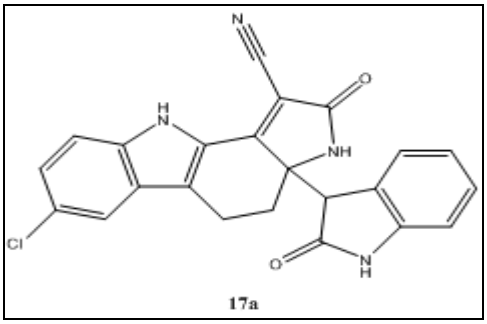


Figure: 15 Compound**17a**

Lianqi Sun et al. (2016) synthesized a Carbazole Sulfonamide Derivatives. The compound were evaluated for in-vitoantitumour activity against different cell lines HepG2 cells (hepatoma cancer), MCF-7 (breast cancer), MIA PaCa-2 (pancreatic cancer), and Bel-7402 (hepatoma/liver cancer) by MTT assay using podophyllotoxin as standard drug.The result shows that new compounds 13f and 13i as potential potent antitumor activity[21].

Antidiabetic activity

ShaziaIqbal et al. (2017) synthesized a series of Newcarbazole linked 1,2,3-triazoles derivatives. The compounds were evaluated for in-vivo anti-diabetic activity by using α-glycosidase inhibition assay &acarbose used as standard drug. The compound were also tested for in-vitro cytotoxic activity against 3T3 (Mouse fibroblast) cell lines by MTT assay using cycloheximide as standard drug.The results shows that Compounds 7, 9, 10, 19, 20, and 23–26, showed a better activity than the standard α-glycosidase inhibitory drug, acarbose.. Compounds**18a** (IC50 = 1.0 ± 0.057 lM) and **18b** (IC50 = 0.8 ± 0.01 lM) were found to be most active among the series All the compounds 2–27 were found inactive, when tested for cytotoxicity against3T3 cell lines, except a subset of four compounds (6, and 14–16)[22].

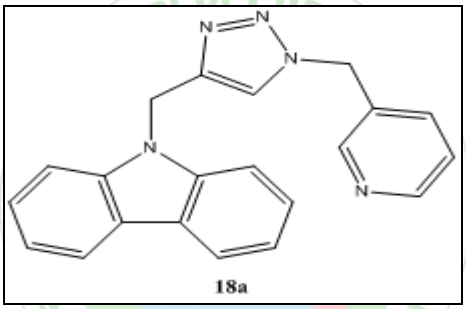


Figure: 16 Compound**18a**

Ji-Quan Zhang et al. (2018) synthesized a series of tetrahydrocarbazole derivatives. The compound were tested for in-vivo Hypoglycemic & hypolipemic activities against human hepatoma cell lines (HepG2) by Glucose consumption assay using DMSO, metformin used as standard drugs. The result shows that compound 7a exhibited hypoglycemic and hypolipemic activity[23]

Antituberculosis activity :

CarstenBörger et al. (2017) synthesized a series of 49 oxygenated tricyclic carbazole derivatives. The compounds were tested for in-vitro anti-tuberculosis activity against Mycobacterium tuberculosis strain $H_{37}Rv$ by the Micro plateAlomar Blue Assay (MABA) & Isoniazid and rifampicin (rifampin) used as standard drugs.The results shows that the compound **19a** exhibit the anti-TB activity[24].

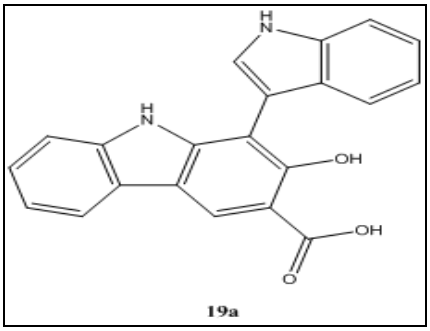


Figure: 17 Compound**19a**

Antiviral activity:

Gerasimos Rassias et.al. (2019) synthesized carbazole derivatives. The compounds were tested for in-vitro anti-viral activity against ZIKV NS3pro by inhibition assay using[25].

Neuroprotective activity:

Roshanak Ghobadian, et. al. (2018) synthesized tetrahydrocarbazole benzyl pyridine hybrids. The compounds were tested for in-vitro neuroprotective activity against Butyryl cholinesterase (BuChE) inhibitors by Ellman's method using Donepezil as a standard drug. The result shows that compound **20a** (IC50 = 0.088±0.0009μM) exhibitthe most potent BuChE inhibitor[26].

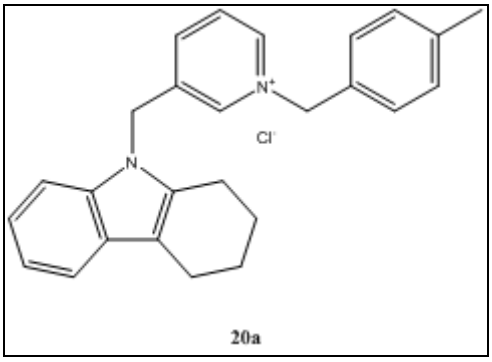


Figure: 18 Compound **20a**

Antiplasmodial and antischistosomal activities:

Weisi Wang et al. (2017) synthesized carbazole amino alcohols derivatives. The compounds were tested for in-vitro anti-plasmodial and antischistosomal activity against Plasmodium falciparum 3D7 and Dd2 strains and adult and juvenileSchistosoma japonicum.by P. falciparum whole cell assay using Chloroquine and dihydroartemisinin as stanadard drugs.The result shows that the compound **21a** exhibit potent dual anti-parasitic activities[27].

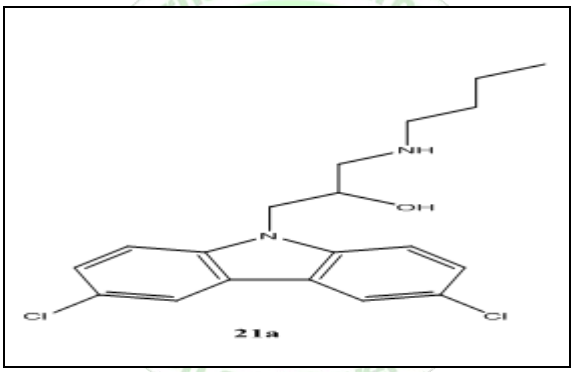


Figure: 19 Compound **21a**

REFERENCE

1. Achab, S. et. al. A short route of functionalized imidazo[4,5-c]carbazoles. Synthesis of the first example of the imidazo[4,5-c]β-carboline ring system. Tetrahedron Letters, 2001; 42:8825-8828.
2. Asche, C. et. al. Synthesis-activity relationship of 5H-benzo[b]carbazoles. Bioorganic and Medicinal Chemistry, 2005; 13:819-837.
3. Barbieri, V. et. al. Microwave-assisted one-pot synthesis of substituted tetrahydrocarbazole and 8, 9, 10, 11-tetrahydro-7H-pyrido[α]carbazoles. Tetrahedron Letters, 2006; 47:8289-8292
4. Barta, T.E. et. al., Novel carbazole and acyl-indole anti-mitotics. Bioorganic and Medicinal Chemistry, 2009; 19:3078-3080.
5. Baumann, S. et. al. NSAID-derived γ-secretase modulators. Part III: Membrane anchoring. Bioorganic and Medicinal Chemistry Letters, 2009; 19:6986-6990.
6. Becknell, N.C. et. al. Novel C-3 N-urea, amide, and carbamatedihydroindazolo[5,4-α]pyrrolo[3,4-c]carbazoleanalogs as potent TIE-2 and VEGF-R2 dual inhibitors. Bioorganic and Medicinal Chemistry, 2006; 16:536.
7. Bedford, R.B. et. al. N-H Carbazole synthesis from 2-chloroanilines via consecutive amination and C-H activation. Journal of Organic Chemistry, 2006; 71:9403-9410.
8. Bedford, R.B. et. al. Intramolecular direct arylation in the synthesis of fluorinated carbazoles. Tetrahedron, 2008; 64:6038-6050.
9. Bergman, J.et. al.Synthesis of carbazole alkaloids. Pure & Applied Chemistry, 1990; 62(10):1967-1976.
10. Bianchi L. et. al.An original route to newly-functionalized indoles and carbazoles starting from the ring-opening of nitrothiophenes. Tetrahedron Letters, 2012; 53:752-757.
11. Nadia Salihet. al. Synthesis and antimicrobial activities of 9H-carbazole derivatives, Arabian Journal of Chemistry, 2016; 9:S781–S786.
12. Ahmad H. Abdullah et.al. Synthesis and antibacterial activity of N1-(carbazol-3-yl)amidrazones incorporating piperazines and related congeners, Z. Naturforsch. 2016; 71(8)b;857–867
13. Entesar M. Ahmed et.al. Towards breast cancer targeting: Synthesis of tetrahydroindolocarbazoles, antibreast cancer evaluation, uPA inhibition, molecular genetics and molecular modelling studies, Bioorganic Chemistry, 2019; 93:103332
14. Pramod V. Chavan et.al. Click chemistry based multicomponent approach in the synthesis of spirochromenocarbazole tethered 1,2,3-triazoles as potential anticancer Agents, Bioorganic Chemistry , 2019; 85:475–486
15. Peng-Hui Li et. al. Synthesis of carbazole derivatives containing chalconeanalogs as non-intercalative topoisomerase II catalytic inhibitors and apoptosis Inducers, European Journal of Medicinal Chemistry, 2018; 145:498-510
16. aGng Li et. al. One-step synthesis of methylene-bridged bis-carbazole and evaluation of its antitumor activity and G-quadruplex DNA binding property, Bioorganic Chemistry, 2019; 90:103074
17. Karunanidhi Murali et.al. Synthesis of hetero annulated isoxazolo-, pyrido- and pyrimidocarbazoles: Screened for in vitro antitumor activity and structure activity relationships, A novel 2-amino-4-(3'-bromo- 4'-methoxyphenyl)-8-chloro-11H-pyrimido[4,5-a]carbazole

as an antitumor, European Journal of Medicinal Chemistry, 2017; 30071(5):S0223-5234

18. KarunanidhiMurali et.al. Regioselective synthesis and stereochemical structure of anti-proliferative active dispirooxindole-pyrrolo-carbazole hybrids via 1,3-dipolar cycloaddition reactions, European Journal of Medicinal Chemistry, 2017; 30942-X:S0223-5234
19. Takashi Nishiyama et.al. Concise synthesis of carbazole-1,4-quinones and evaluation of theirantiproliferative activity against HCT-116 and HL-60 cells, European Journal of Medicinal Chemistry, 2016; 121:561-577
20. PerumalSathiyachandranet. al. Design and synthesis of novel pyrrolo[2,3-a]carbazoles: 7-Chloro-2-oxo-3a-(2'-oxo-2',3'- dihydro-1'H-indol-3'-yl)-2,3,3a,4,5,10-hexahydro-pyrrolo[3,2-a]carbazole-1-carbonitrile as an efficient anticancer agent, , European Journal of Medicinal Chemistry, 2018; 30299-X:S0223-5234
21. Lianqi Sun et. al. Novel CarbazoleSulfonamide Derivatives of Antitumor Agent: Synthesis, Antiproliferative Activity and Aqueous Solubility, Bioorganic & Medicinal Chemistry Letters, 2016; S0960-894X:31214-8
22. ShaziaIqbal et.al. New carbazole linked 1,2,3-triazoles as highly potent non-sugar a-glucosidase inhibitors, Bioorganic Chemistry, 2017; 74:72–81
23. Ji-Quan Zhang et. al. Discovery of tetrahydrocarbazoles with potent hypoglycemic and hypolipemic Activities, European Journal of Medicinal Chemistry, 2018; 30206-X:S0223-5234
24. CarstenBörgeret. al. Anti-tuberculosis activity and structure–activity relationships of oxygenated tricyclic carbazole alkaloids and synthetic derivatives, Bioorganic & Medicinal Chemistry, 2017; 25:6167–6174
25. GerasimosRassiaset. al. Cell-active carbazole derivatives as inhibitors of the zika virus Protease, , European Journal of Medicinal Chemistry, 2019; 180:536-545
26. RoshanakGhobadianet. al. Novel tetrahydrocarbazole benzyl pyridine hybrids as potent and selective butryl cholinesterase inhibitors with neuroprotective and β-secretase inhibition activities, , European Journal of Medicinal Chemistry, 2018; 30444-6:S0223-5234
27. Weisi Wang et. al. Novel carbazoleamino alcohols as inhibitors of b-hematin formation: Anti-plasmodial and anti-schistosomal activities, International Journal for Parasitology: Drugs and Drug Resistance , 2017:191-199.