BIOLOGICAL POTENTIAL OF INDOLE DERIVATIVES IN RECENT RESEARCH

Ashok Kumar Yadav, Mukesh Kumar Shukla*,Razia Bano

Hygia Institute of Pharmaceutical Education and Research, Sitapur- Hardoi Bypass Road, Opp. Sahara City Homes, Prabandh Nagar, Lucknow, Uttar Pradesh, India 226013

Corresponding author:

Abstract

Numerous indole-containing bioactive aromatic molecules shown biological and medical uses. Numerous significant synthetic medicine compounds contain the indole scaffold, which provided a useful treatment notion and binds with high affinity to a variety of receptors to aid in the development of novel beneficial derivatives.Because of the physiological actions that indole derivatives have, such as their antiviral, anti-inflammatory, anticancer, anti-HIV, antioxidant, antimicrobial, ant tubercular, antidiabetic, antimalarial, and anticholinesterase properties, researchers have been interested in synthesizing a range of indole derivatives.

According to the literature, indole derivatives offer a wide range of biological functions and enormous promise for research into additional medicinal applications.

Keywords: Antiviral, Anti-Inflammatory, Anticancer, Antioxidant, Antimicrobial, Tuberculosis-Fighting, Anti-Diabetic, Anti-Malarial, and Anticholinesterase.

I. INTRODUCTION

Indole is also referred as benzo pyrrole, which has a benzenoid nucleus and contains 10 -electrons (two from a lone pair on nitrogen and eight from double bonds), making it naturally aromatic. Due to high -electrons delocalization, indole rapidly undergoes electrophilic substitution, much like the benzene ring does.

The skeleton for substances like lysergic acid diethylamide (LSD), strychnine, and plant-derived alkaloids is provided by the significant heterocyclic system known as indole. Physically, they are colorless crystals with distinctive scents. It became a significant heterocyclic molecule with

broad-spectrum biological effects when the indole nucleus was added to pharmaceutical compounds with biological activity.

We are aware that the categorization of pathways for indole manufacture has been on organic chemists' thoughts for more than a century as we proceed. Indole synthesis has been the subject of several reviews. 1 In addition, we were conscious that much more could be written than what we have. The reduction of oxindoles to indoles and the conversion of indoles to indoles have only been slightly discussed. The considerable literature on altering already-existing indoles has not been explored by us. Our goal has been to provide examples rather than an entire list of everything. However, it is clear that any indole synthesis must adhere to one of the nine here-mentioned strategic methods. The global research effort is unified and organized through the network of scientific citations. We hope that the classification scheme proposed here for indole syntheses will be widely accepted. By categorizing their technique, writers will be able to quickly learn about the past and present state of the art for that method of indole production as they develop novel approaches to the indole nucleus. Our goal is that by reducing redundancy, efforts will then be focused on the very real obstacles that still need to be solved. It is remarkable that each of these nine techniques reported significant new contributions in 2009, the most recent year we have reviewed.

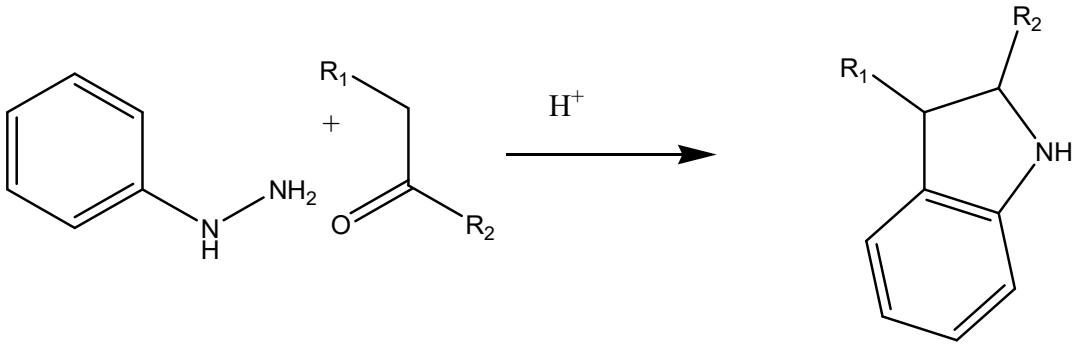
As a result, scientists were interested in synthesizing different indole scaffolds to screen for varied pharmacological actions. Indole is the parent nucleus of several natural chemicals, including tryptophan. A plant hormone called indole-3-acetic acid is created when tryptophan is broken down in higher plants. Indole derivatives are of great interest due to their numerous biological and medical uses. Here, we've attempted to condense the key pharmacological functions of indole derivatives.

II. METHODS OF SYNTHESIS OF INDOLE

There are several name reactions associated with indole synthesis. A few of the name reactions are mentioned below.

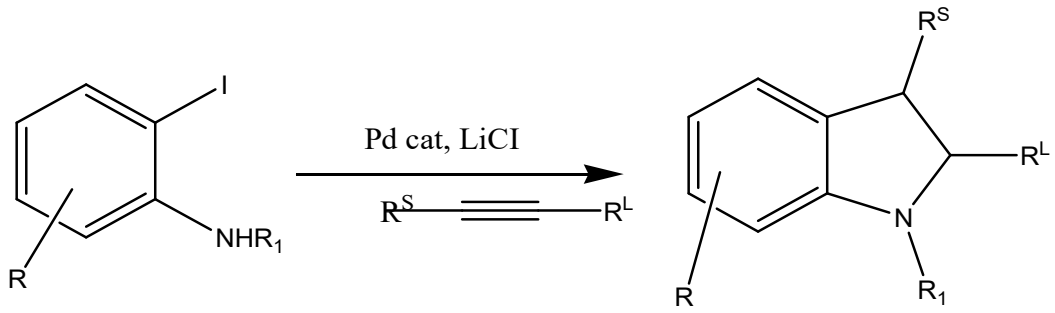
Fischer Indole synthesis

This method entails heating phenyl hydrazine with an aldehyde or ketone in an acidic environment, forming phenyl hydrazine, which then undergoes a reaction with a lack of alkali to produce an indole or 2- and 3-substituted indoles.



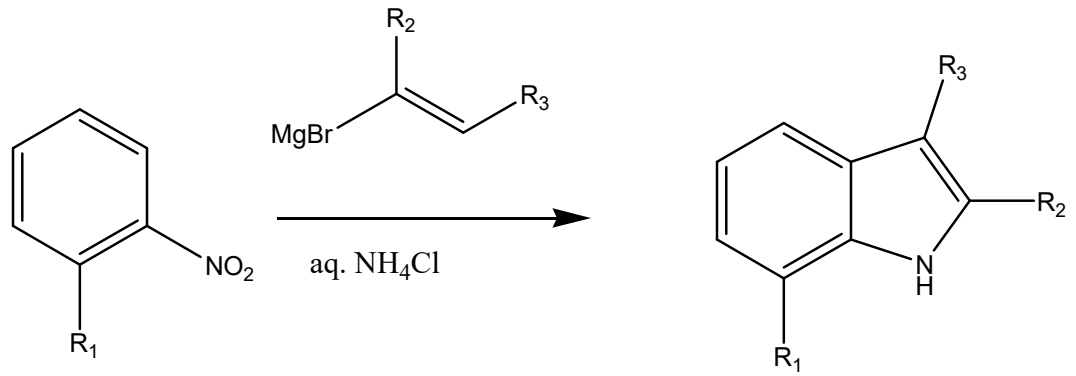
Cyclization of2-Alkynylanilines

The Larock heteroannulation reaction is referred to as the palladium-catalyzed reaction between the o-iodoaniline compound and inner alkynes to the building of 2,3-disubstituted indolyl ring.



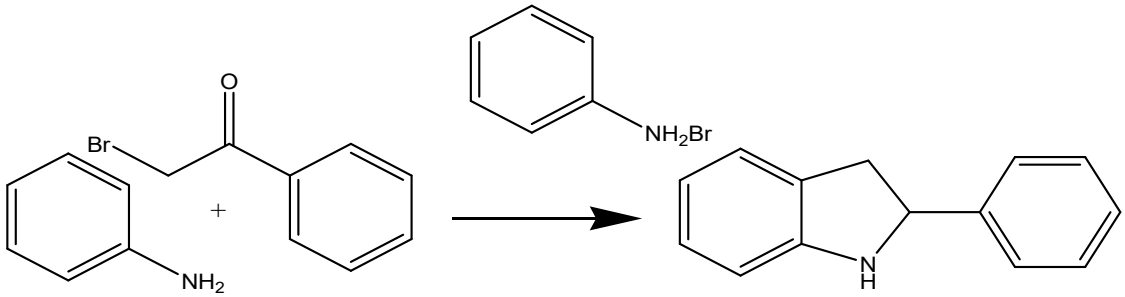
Bartoli indole synthesis

Subbed indoles are obtained in the Bartoli indole union by reacting ortho-subbed nitroarenes with vinyl Grignard reagents.



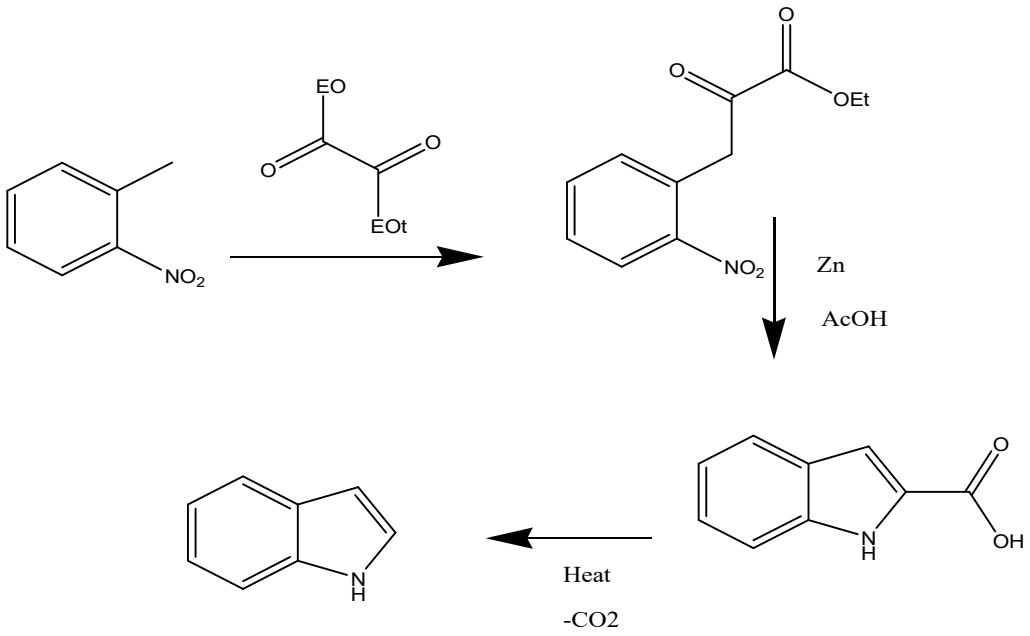
Bischler Synthesis

This method involves a simple reaction of an α-bromo-acetophenone and excess aniline leading to the formation of 2-aryl indole.



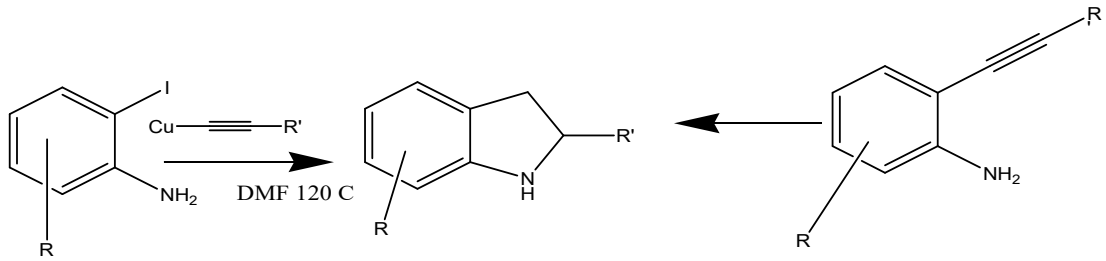
Reissert synthesis

In 1897, Reissert published a study on the synthesis of indole using orthonitrotoluene and diethyl oxalate. The classic Reissert indolyl synthesis entails the condensation of o-nitro toluene with an ester frame of oxalic acid to create o-nitro phenylpyruvate, which is hindered by ring reduction to indole-2-carboxylic corrosive subordinates.



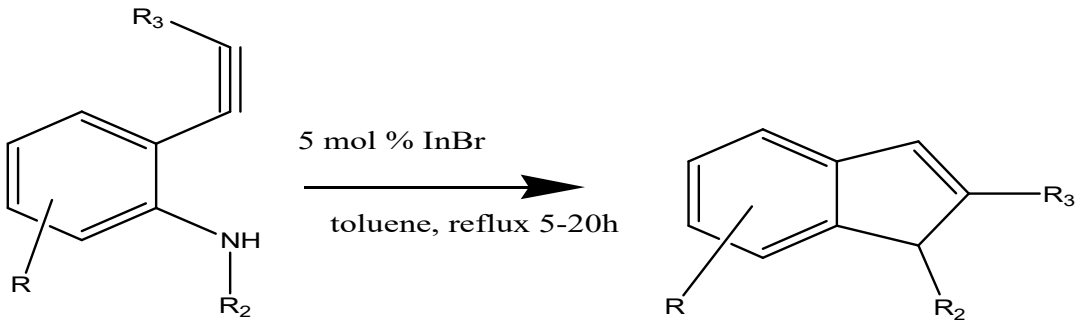
Castro Indole synthesis

Additionally, o-iodoanilines subordinated to cuprous acetaldehyde or 2-alkynylanilines to copper (I) combinations, often copper iodide, are included in the Castro indolyl union. For the synthesis of indoles, the copper-advanced cyclization of 2-alkynylanilines stands out as an appealing method.



Sakai synthesis

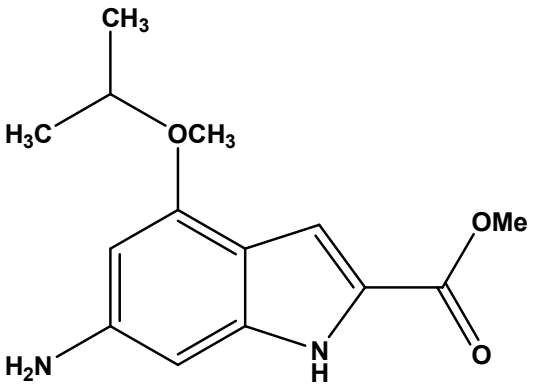
Several indole derivatives have been synthesized via indium-catalyzed cyclization of 2-ethynylanilines in good yields.



II. BIOLOGICAL ACTIVITIES OF INDOLE

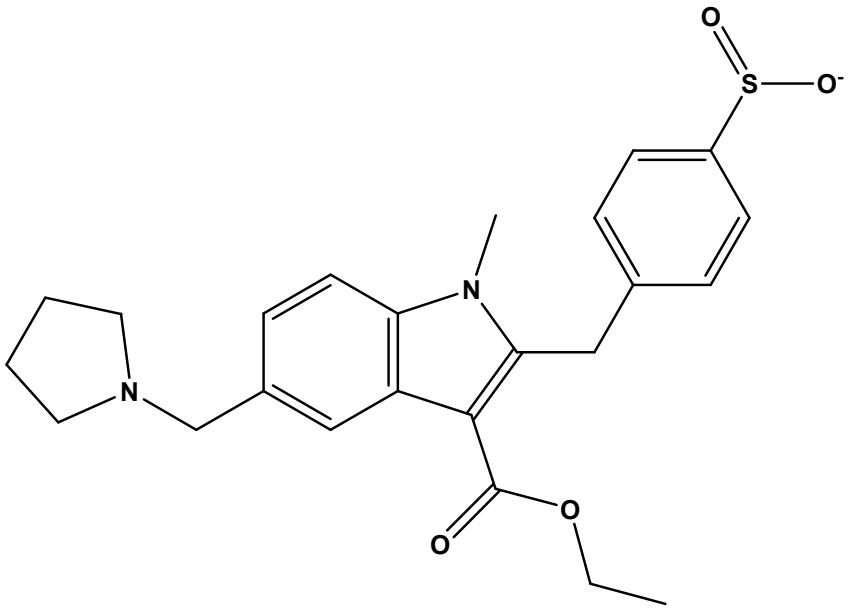
Antiviral

Xue *et al.* synthesized and characterized 6-amino-4-substitutedalkyl-1H-indole-2-substitutedcarboxylate derivative products as antiviral drugs. All of the molecules examined had inhibitory action toward influenza A, with molecule **1a** having the lowest IC50 value (7.53 mol/L) and the greatest selectivity index (SI) rating (17.1) against CoxB3 virus.



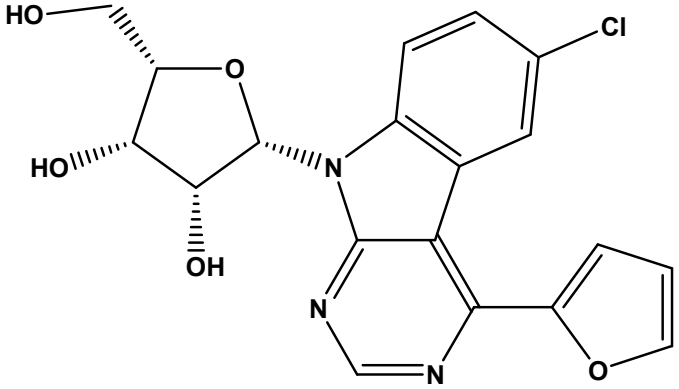
1a

Sellitto *et al.*explained the antiviral action of ethyl 1H-indole-3-carboxylates in Huh-7.5 cells. **1b** The much more effective substance against with the hepatitis C virus at low concentrations was benzenesulfinate.



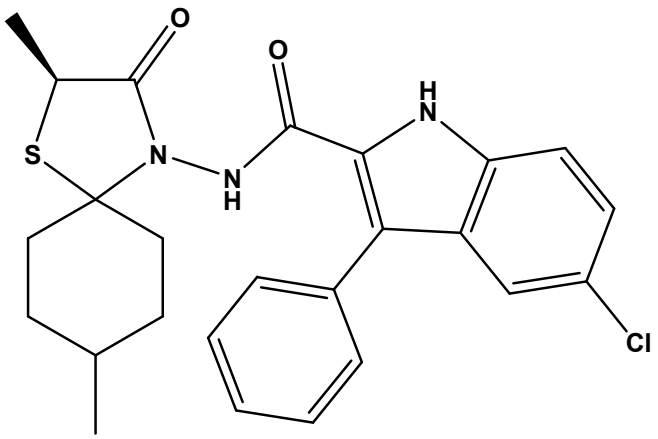
1b

Tichy *et al*. produced and examined -tetrahydrofuran-3,4-diols for in vitro antiproliferative (HL-60 cervical cancer HeLaS3, Tlymphoblastic leukaemia human cell line CCRF-CEM, and promyelocytic leukaemia) and antiviral activity (Dengue virus and anti-hepatitis C virus) **1c**With an IC50 of 0.175 and 1.565 M, -tetrahydrofuran-3,4-diol (8) showed substantial cytotoxicity in HepG2 cells and THP-1.



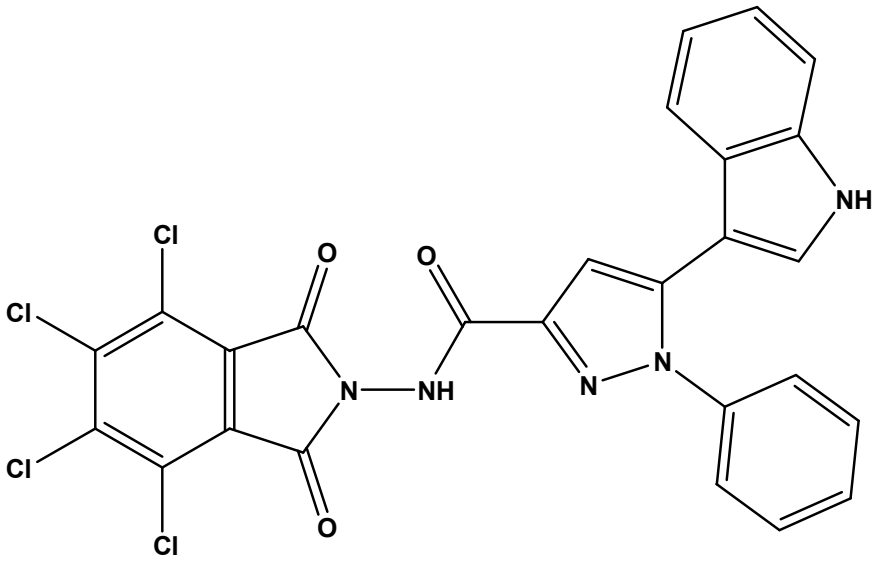
1c

Cihan-Üstündag *et al.* synthesised and tested **1d** derivatives of indole for antiviral activity in vitro against a variety of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) viruses. Compounds The antiviral compounds **1d**

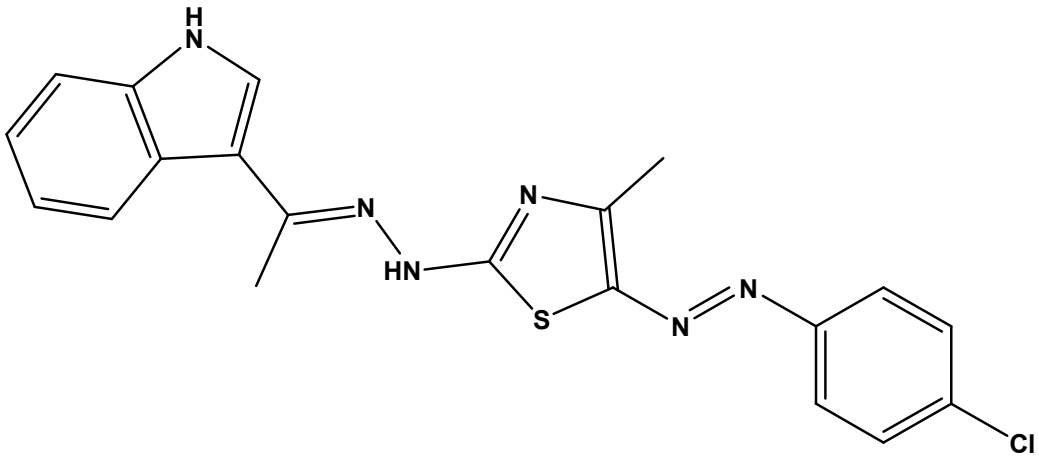


1d

Abdel-gawad *et al.* synthesised 1,3,4-thiadiazine-containing indole nucleus derivatives and evaluated them for their antiviral efficacy against HSV-1 (herpes simplex type 1).Compounds **1e**and **1f**powerful antiviral drugs that exhibit the strongest efficacy against HSV-1 have IC50 values ranging from 0.4 to 2.1 g/mL against Coxsackie B4 virus and 1.565 M.



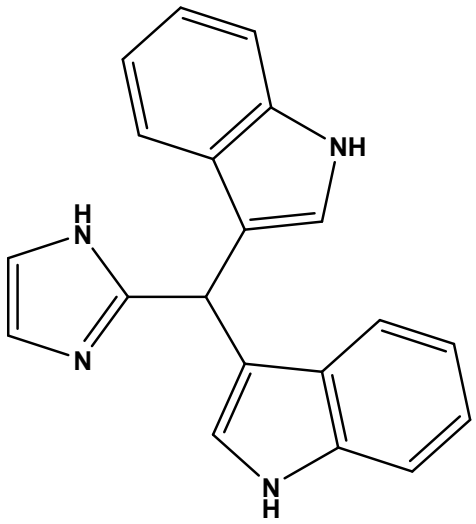
1e



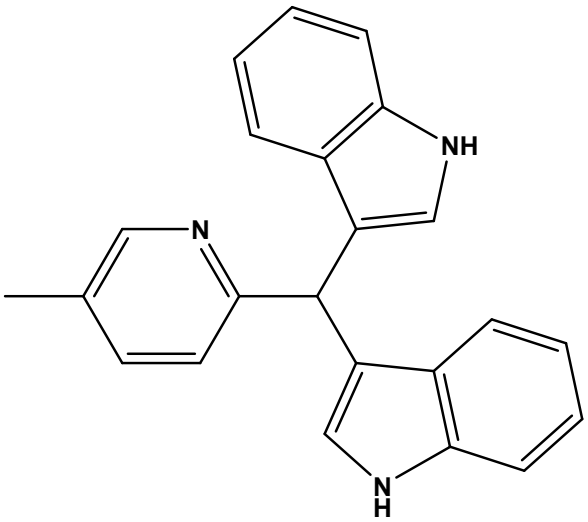
1f

Anti-inflammatory and Analgesic

In a microwave, indole and substituted aldehydes underwent a solvent-free reaction, according to Sarva *et al*. Bis(indolyl)methane, the product, is biologically active. Most of the compounds had anti-inflammatory properties, although **2a** and **2b.**

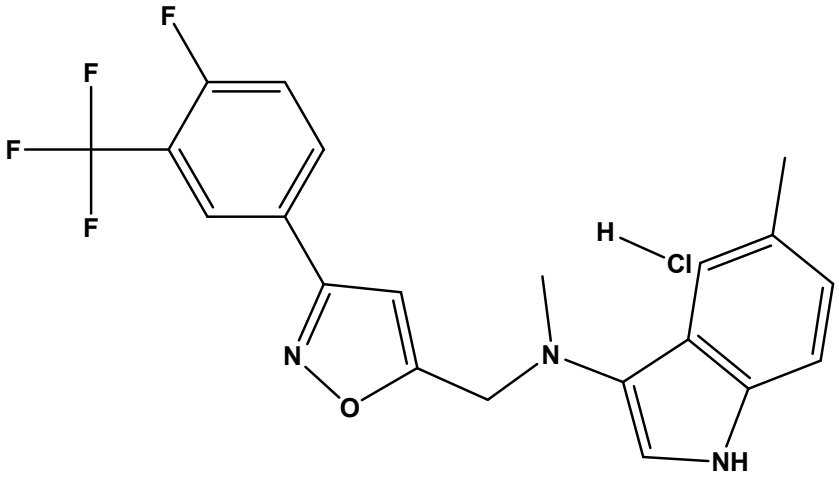


2a



2b

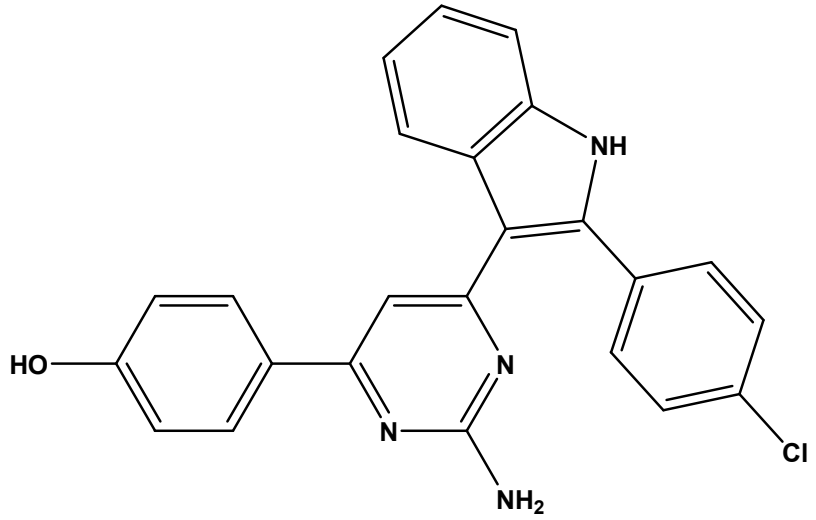
Pedada *et al.* revealed the existence of derivatives of indole that include isoxazole that are sPLA2 inhibiting. Significant sPLA2 inhibitory action was seen with compound **2c** that is equivalent to or greater than ursolic acid (positive control) and 1.565 M.



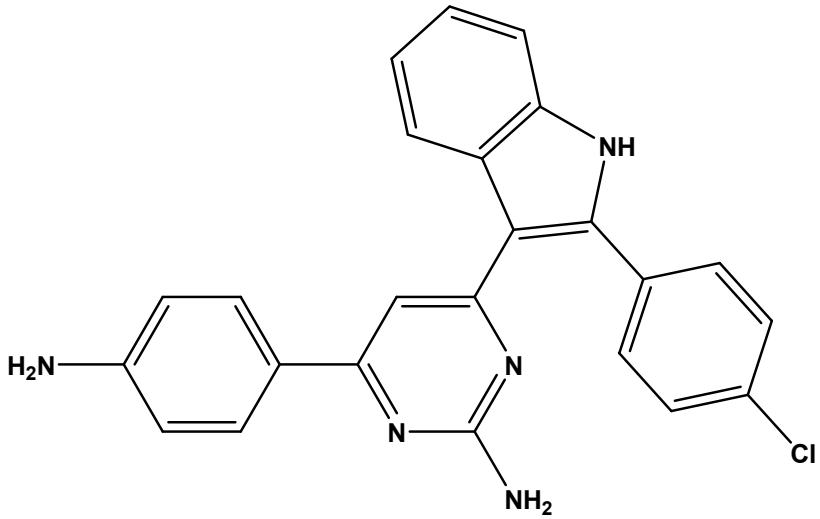
2c

Chavan *et al.* created 3-(2-aminopyrimidin-4-yl) indoles and tested them for their ability to induce ulcers, reduce inflammation, and provide analgesia. With indomethacin, each synthesized molecule exhibited similar results. 4(2- amino) compounds were assessed from all of the

constituents. Both **2d** and **2e** Inhibition of inflammation with paw edoema and pyrimidin-2-amine demonstrated 87.4 and 88.2% and 78.5 and 76.6%, respectively.

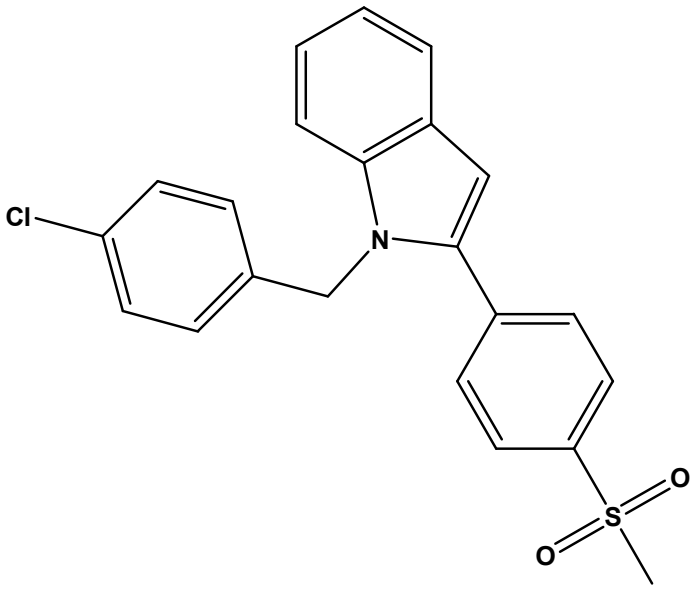


2d

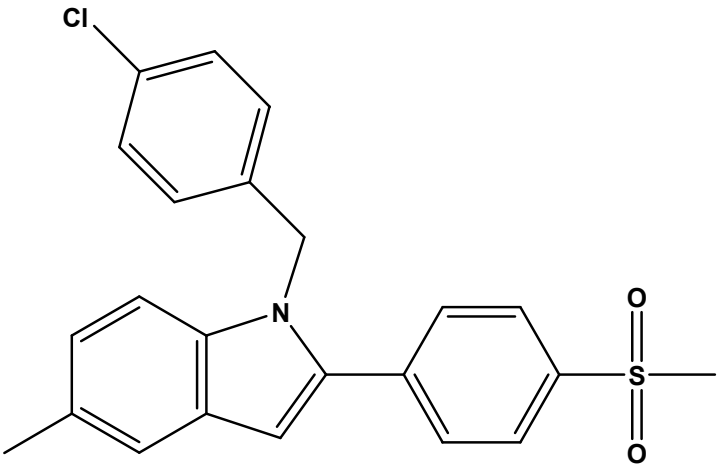


2e

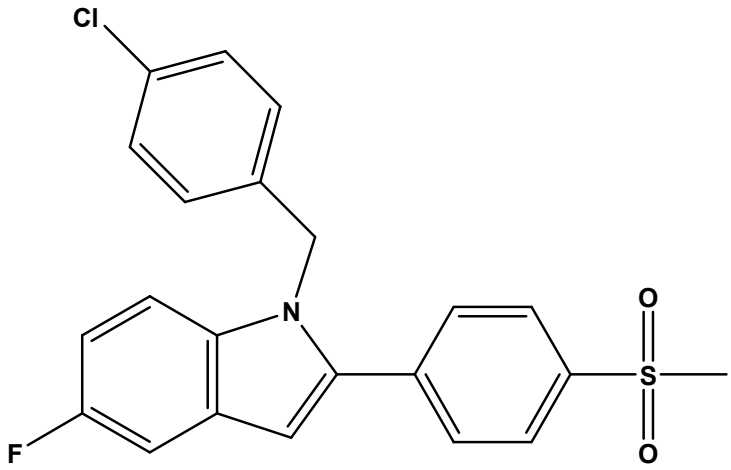
Shaker *et al.* created -1-substituted-indole and tested it for both in vivo and in vitro COX-2 inhibitory activities.While in vivo anti-inflammatory activity studies revealed substances **2f, 2g,** and**2h**COX inhibitory activity (in vitro) assessment demonstrated preferential binding with receptor (COX-2) with SI = 30.35-107.63 as opposed to conventional medication (SI = 0.079).(75.6%), and (81.1%).



2f



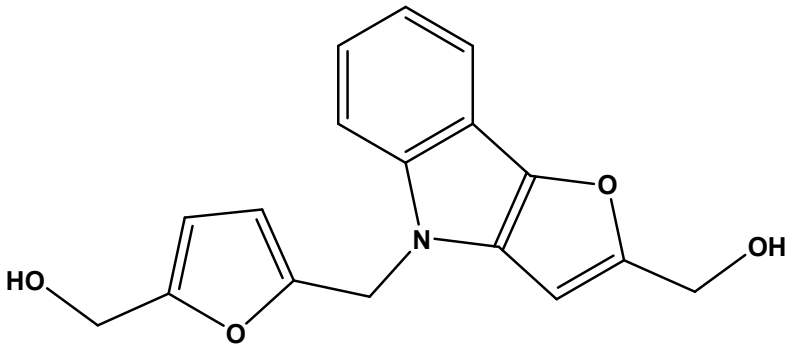
2g



2h

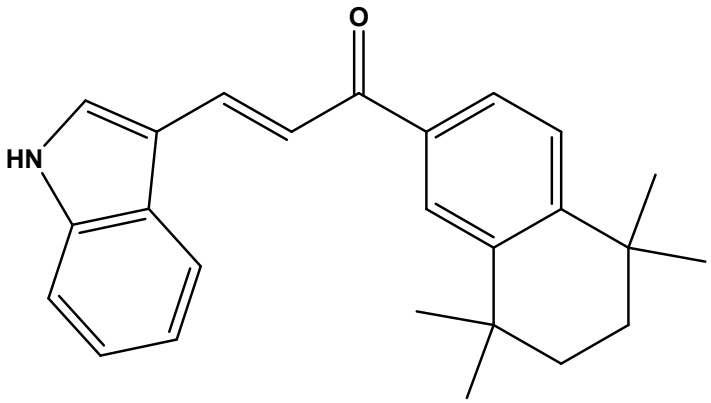
Anti-cancer

A variety of 2, 4-disubstituted furo[3,2-b]indoles were tested for anticancer efficacy against the (human NCI-60) tumour cell lines by Zhuang *et al.* The most effective anticancer action was shown by compound **3a**among the investigated substances. The findings of the research indicate that compound **3a** fingerprint is comparable to NSC754549.



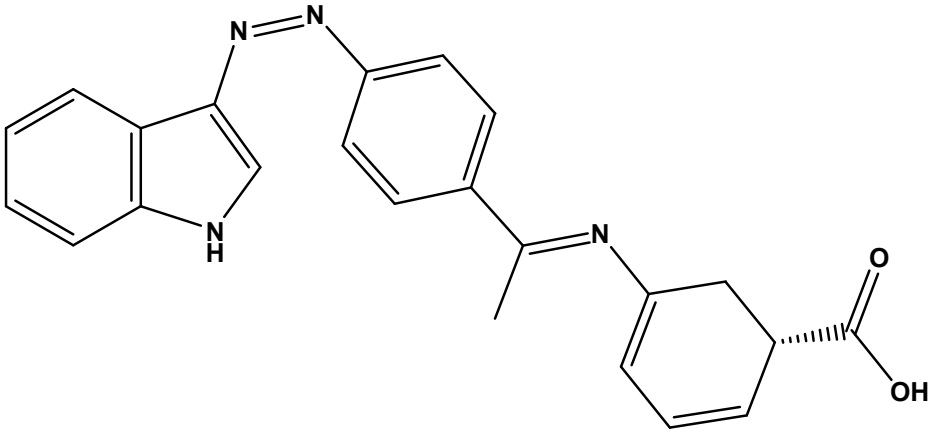
3a

Gurkan-Alp *et al.* synthesised and tested compounds of prop-2-en-1-one for their anticancer properties. The most active compound was determined to be prop-2-en-1-one **3b.**

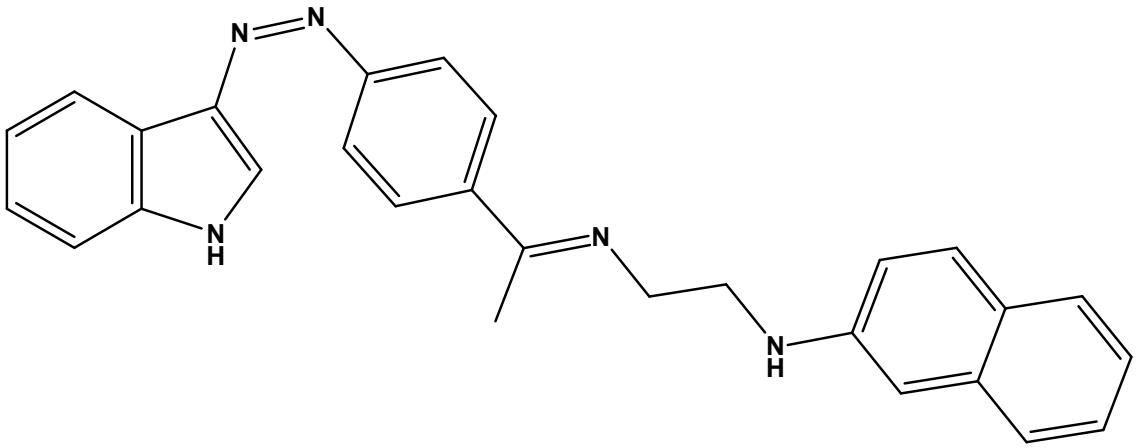


3b

The cytotoxicity of indole hybridised diazenyl derivatives against human cell lines, including leukemic cell (K562), normal cell (HEK293), lung cell (HCT-116), and breast cell, was constructed and reported (MDAMB231) adopting Kaur et alMTT .'s assay. Compounds **3c** and **3d** demonstrated promise in a breast cancer cell line (MDAMB231)



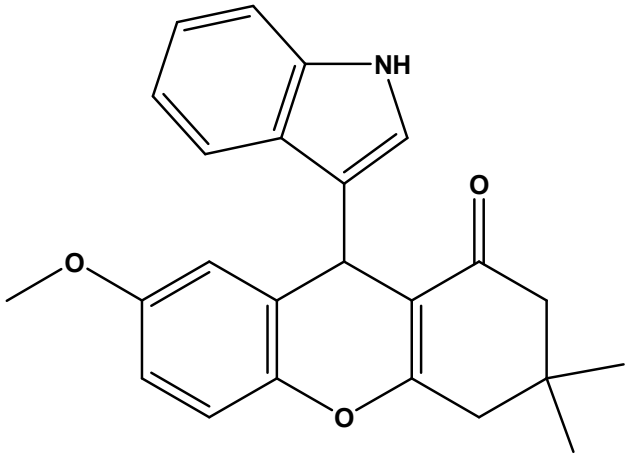
3c



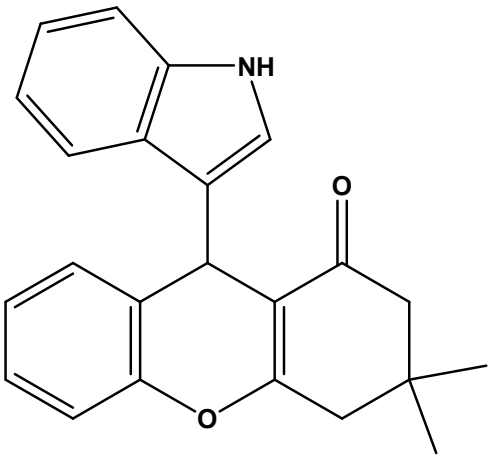
3d

Anti-HIV

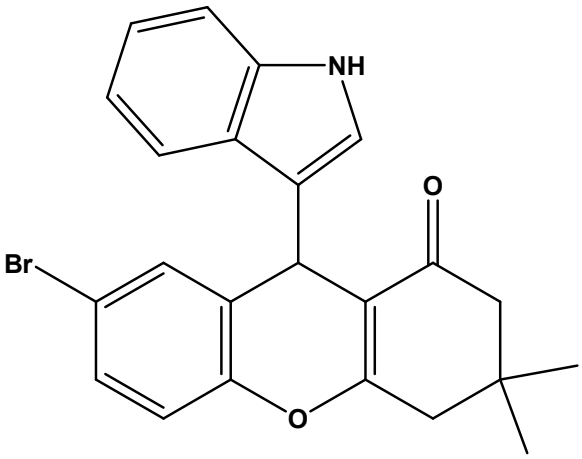
As an anti-HIV-1, Kasralikar et al. performed molecular docking experiments on a number of new indolyl and oxochromenyl xanthenone derivatives. The most active compounds in the studied compounds were **4a, 4b** and **4c.**



4a

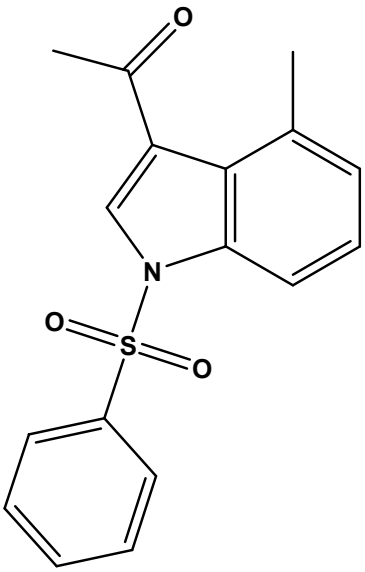


4b

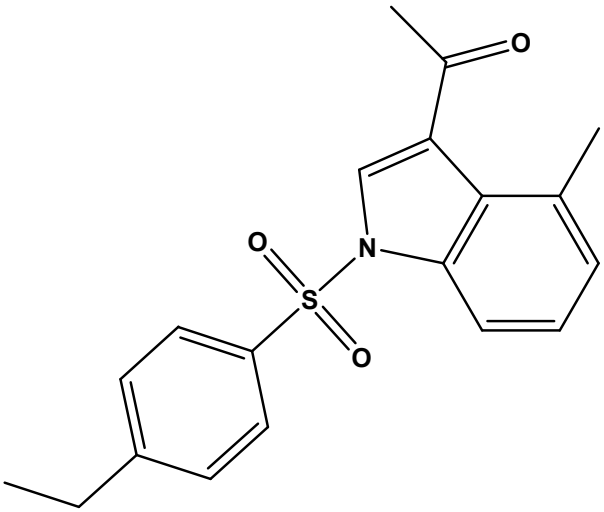


4c

N-arylsulfonyl-3-acetylindole derivative was prepared and evaluated as HIV-1 inhibitors analogs by Ran Et al.Compounds **4c** and **4d** were the most effective against the anti-HIV-1 activity. SAR showed that acetyl group derivatives were more active.

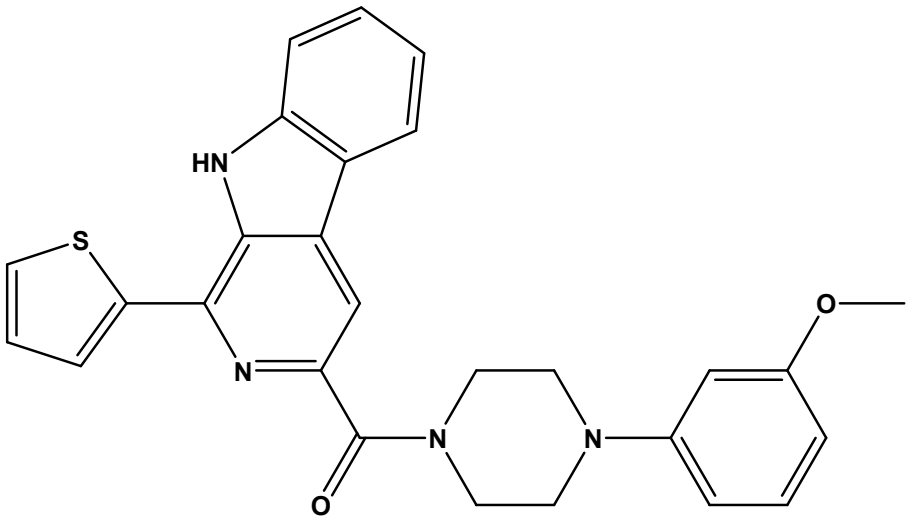


4d



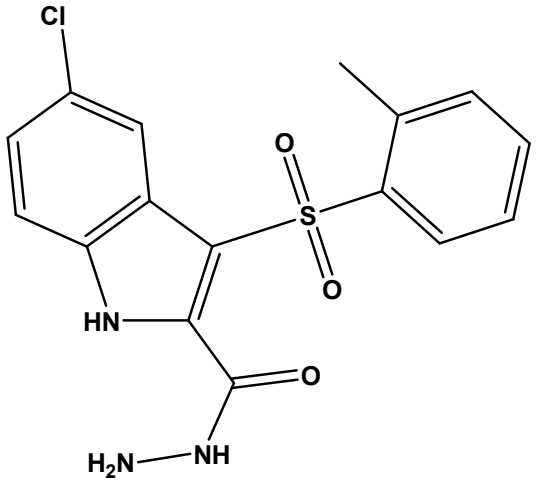
4e

By Ashok *et al.,* 1-(Thiophen-2-yl)-9H-pyrido[3,4-b] indole derivatives were created and tested for their anti-HIV activity. Structure-activity relationship (SAR) analyses revealed that electron-donating ortho, para directing groups and electron-withdrawing group boost the antiviral activities. With a selectivity index (SI) of 483 and an IC50 of 0.53 M, derivative **4f** shown substantial anti-HIV activity. These molecules in the molecular prediction studies adhere to the Lipinski rule (In-silico)

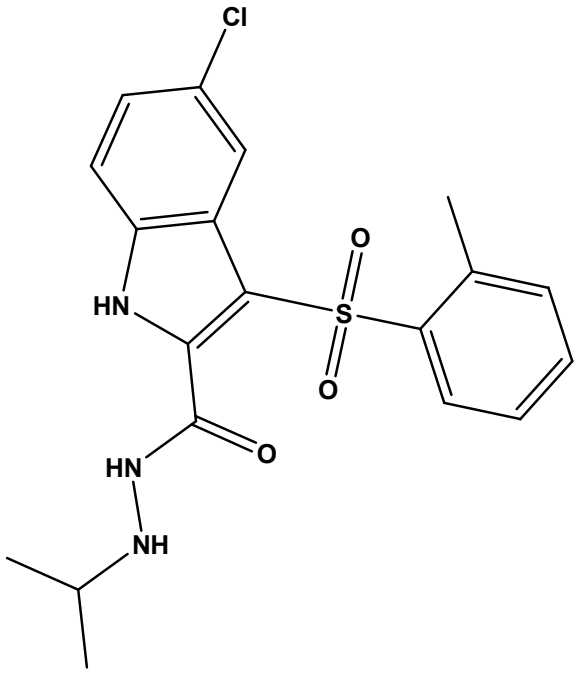


4f

Ragno et al. addressed indolyl aryl sulfones through molecular modelling investigations utilising a 3-D QSAR model as novel antiHIV medicines. The most effective compounds against C-8166 and MT-4 cell were discovered to be **4g** and **4h.**



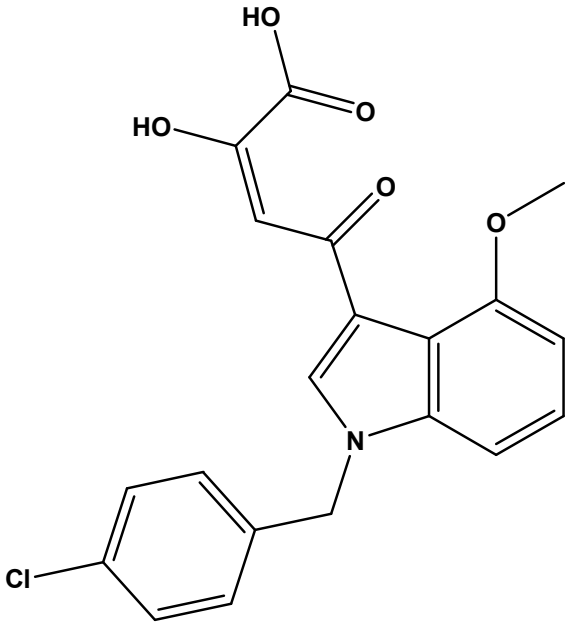
4g



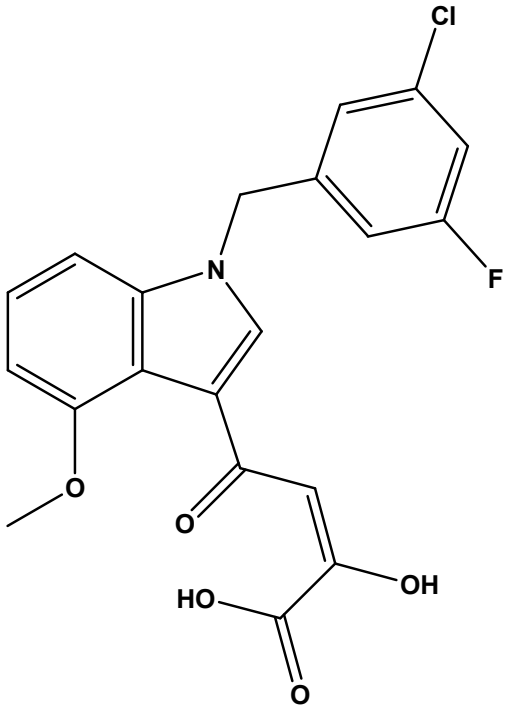
4h

Antioxidant

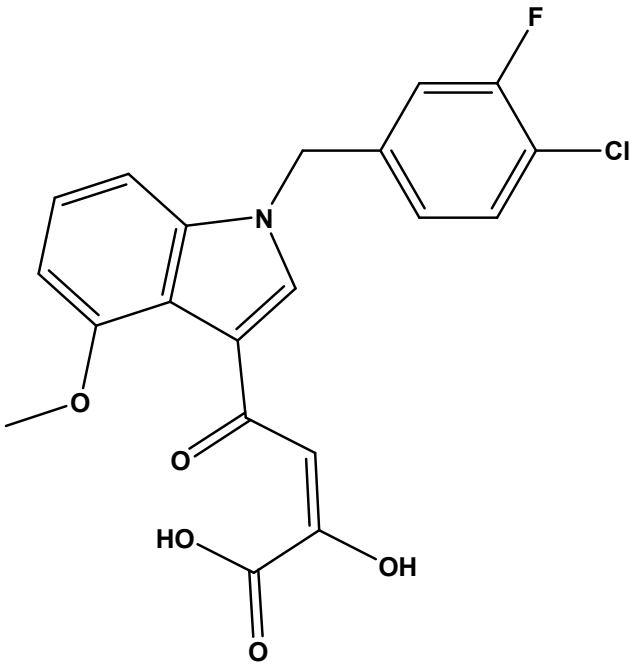
Silveira *et al.* synthesised and tested di(1H-indol-3-yl)sulfane derivatives as antioxidant agents. In ferric reducing ability of plasma (FRAP), 2,2-Diphenyl-1-picrylhydrazyl (DPPH), and 2,2'-Azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) tests, the compounds**5a, 5b** and **5c** shown antioxidant activity.



5a

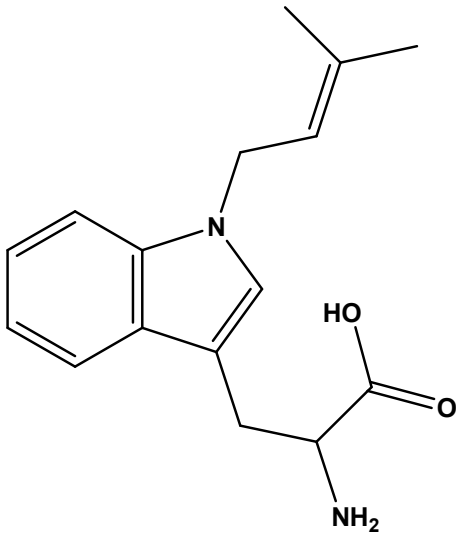


5b

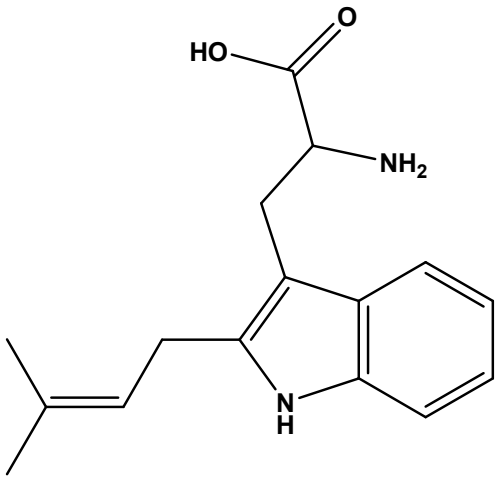


5c

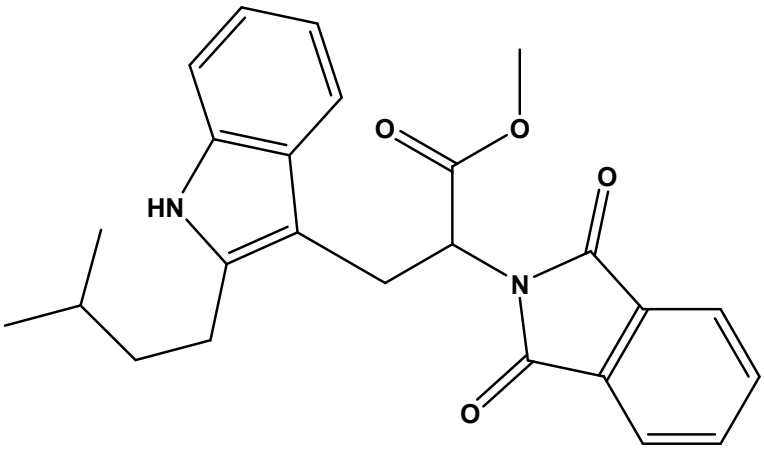
Tryptophan and trypamine are indole derivatives that have been tested for DNA cleavage activity by Estevo et al. Significant activity was observed for the **5d** (IC504.13 0.17 M), **5e** (IC50 4.56 0.48 M), and **5f.**



5d

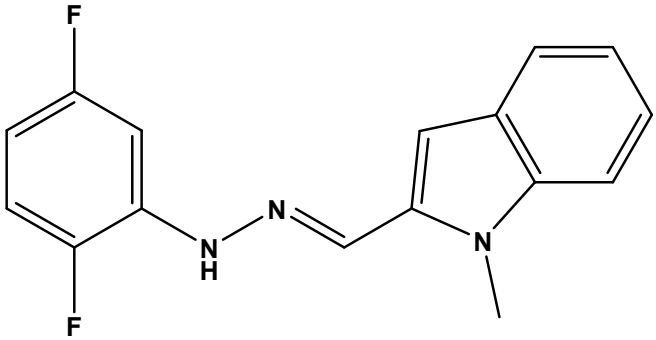


5e

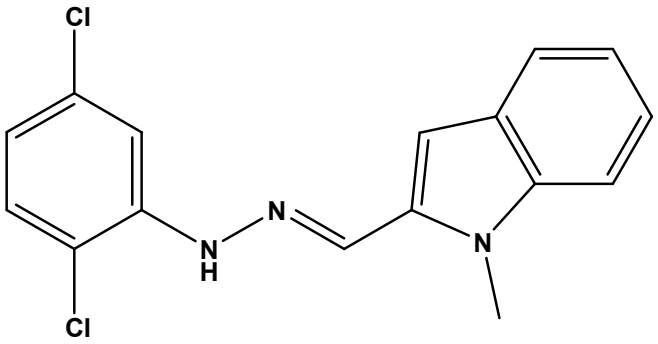


5f

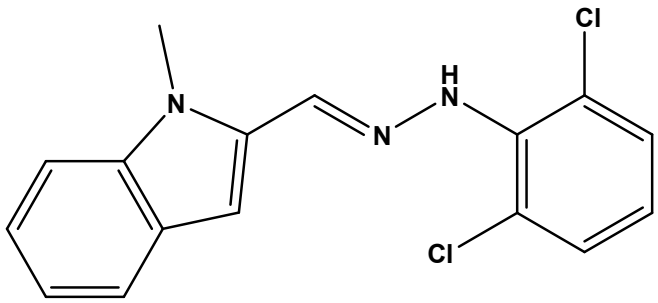
Suzen *et al*. produced and reported the substances **5g,5h** and **5i** The most promising compounds for antioxidant activity.



5g

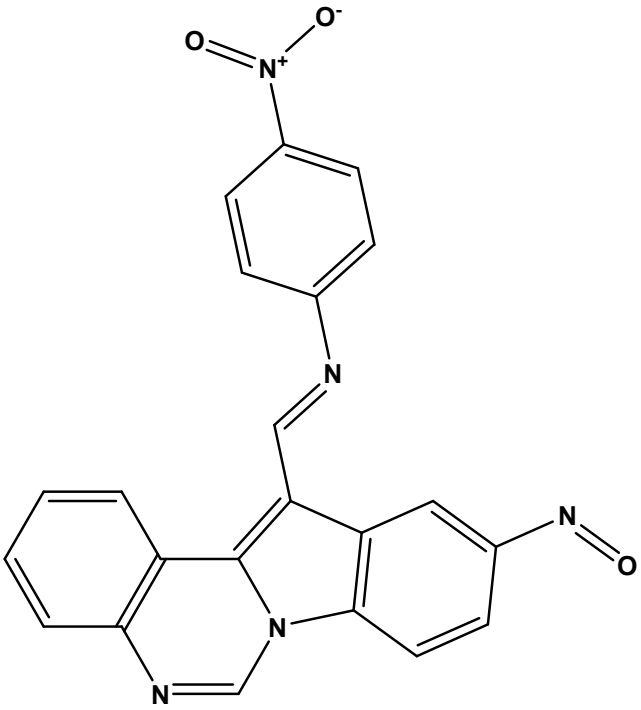


5h

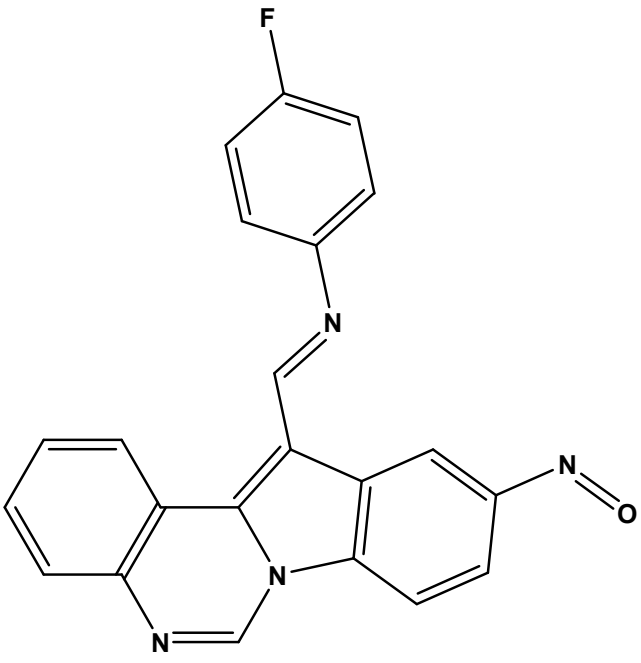


5i

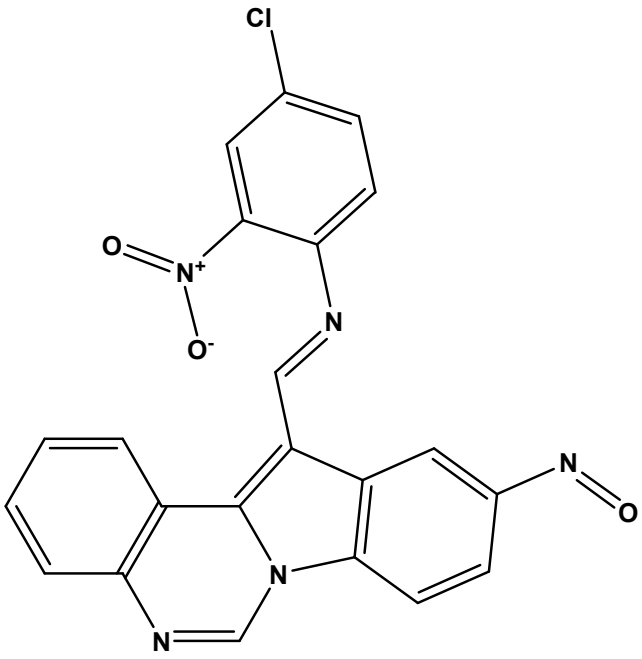
Dixit *et al.* synthesised and evaluated N-((10-nitro-1H-indolo [1, 2-c]quinazolin-12-yl)methylene)benzenamines for their anti-oxidant activities. Nearly all derivatives have demonstrated good antioxidant activity at all concentrations, however **5j, 5k** and **5l.**



5j



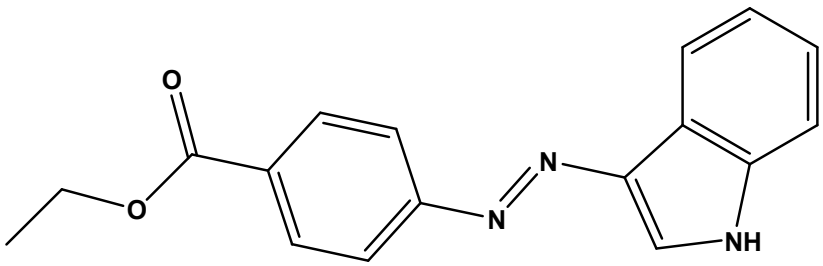
5k



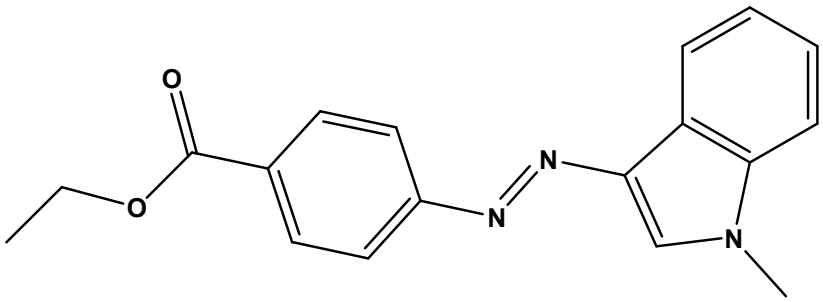
5l

Antimicrobial

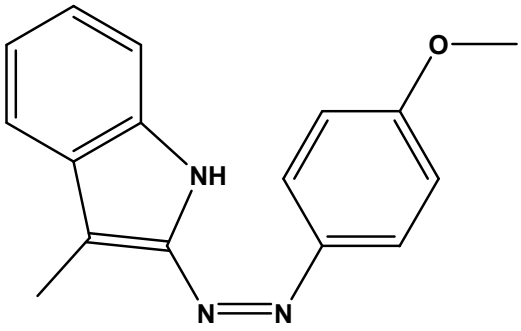
Ozturk *et al.* created an azo dye of indoles and tested it in vitro against yeast Saccharomyces cerevisiae, Gram (+) and (-) bacteria. A number of compounds, including **6a, 6b**and **6c.**



6a

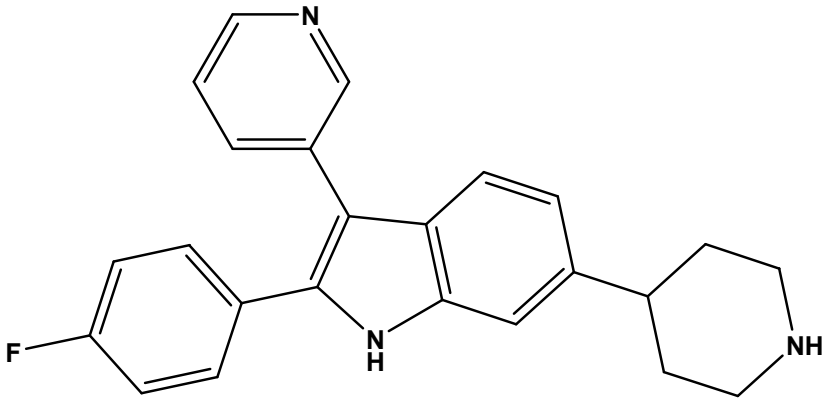


6b



6c

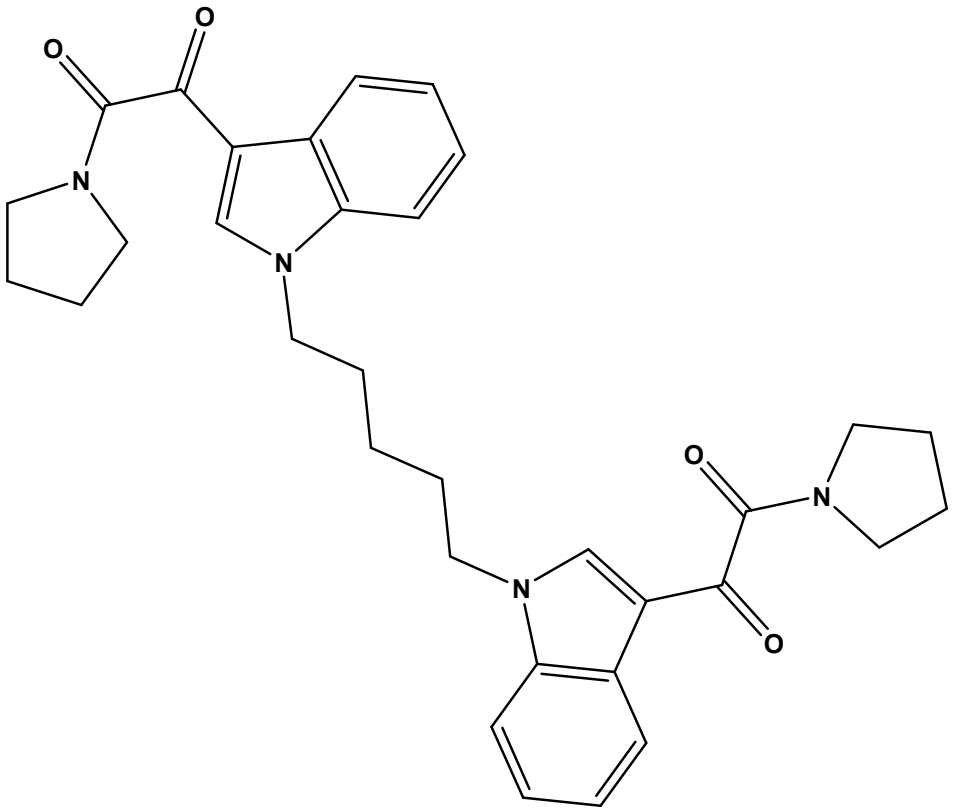
Scribner *et al.* created and tested 2, 3-dialylindole derivatives with amine substituents at the 5 and 6 positions of the indole as anticoccidial drugs. Constituent **5d** was the most active compound.



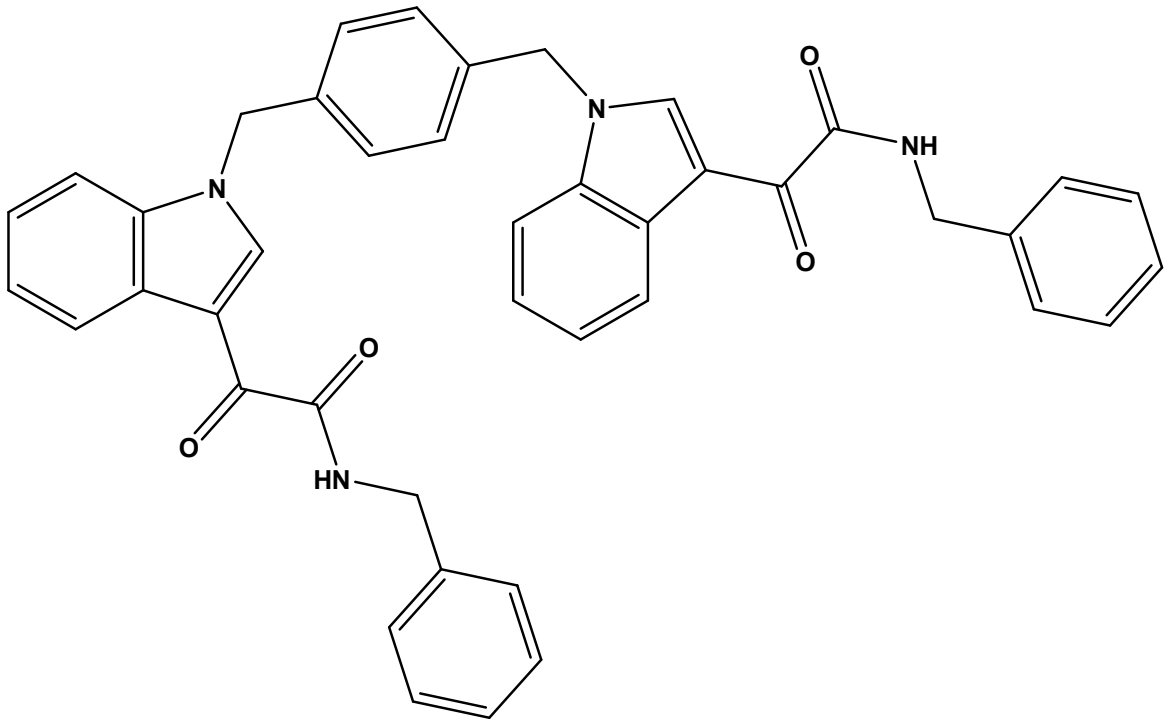
6d

Singh *et al.* synthesised a number of bisindoles with nitrogen and carbon substitutions and tested them as potential antimicrobials. The N-benzyl moiety, morpholine, or pyrrolidine at position 3,

as well as the bridge between the indoles made of xylidine, butane, or propane, were advantageous for activity. Strong connections between the active sites of dihydrofolate reductase and lanosterol demethylase in topoisomerase II were shown by docking experiments. The active compounds (139) and (140)



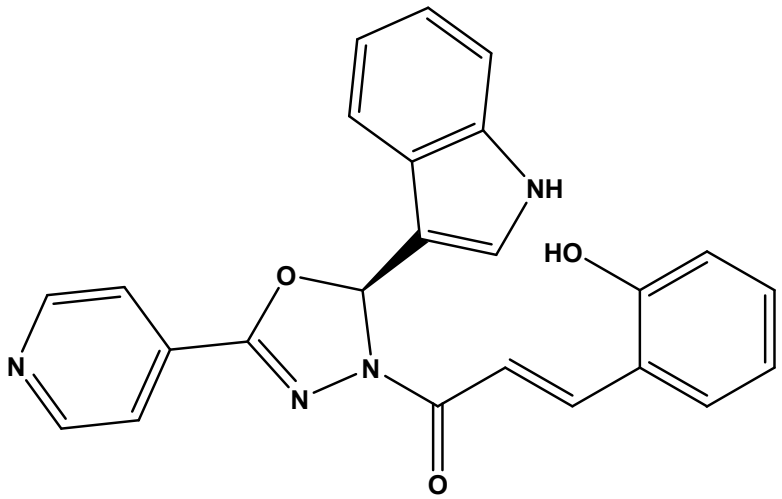
6e



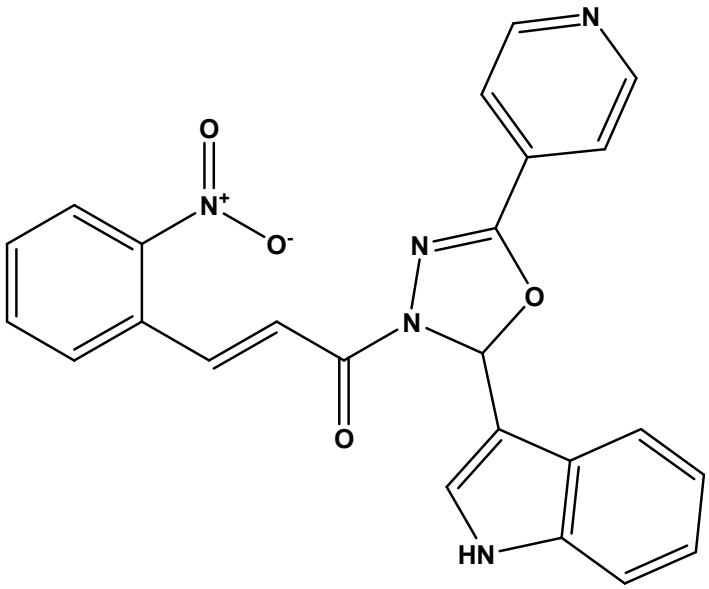
6F

Antitubicular

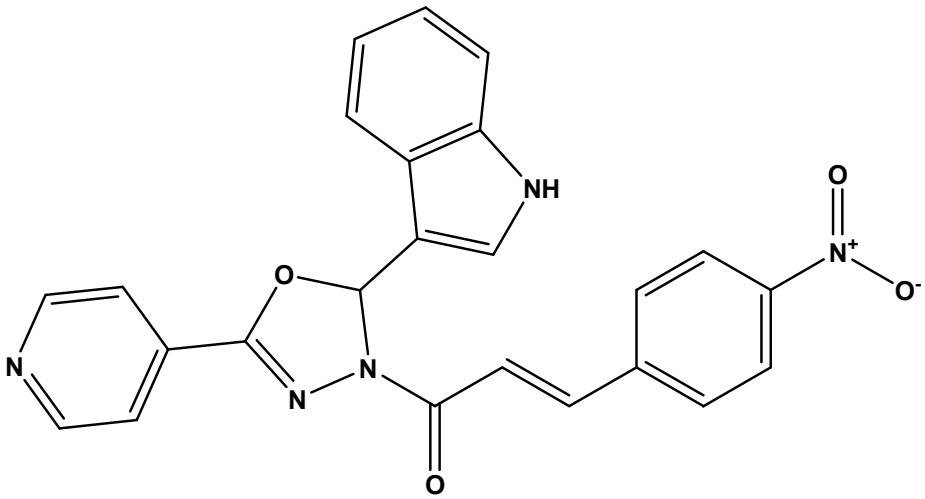
Desai *et al.* synthesised and examined prop-2-en-1-one derivatives generated from pyridine and Indole against H37Ra MTB (Mycobacterium tuberculosis) and BCG (Mycobacterium bovis) for their in vitro antitubercular activities. Effective antitubercular action was shown by **7a, 7b, 7c** and **7d.**



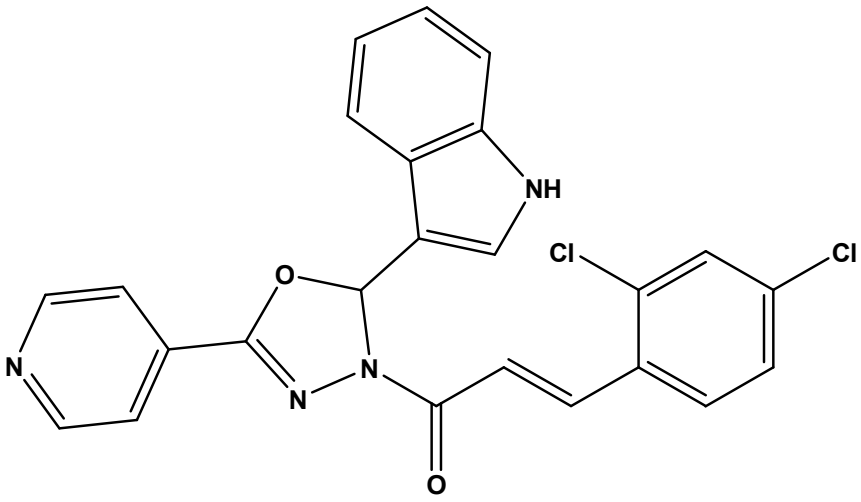
7a



7b

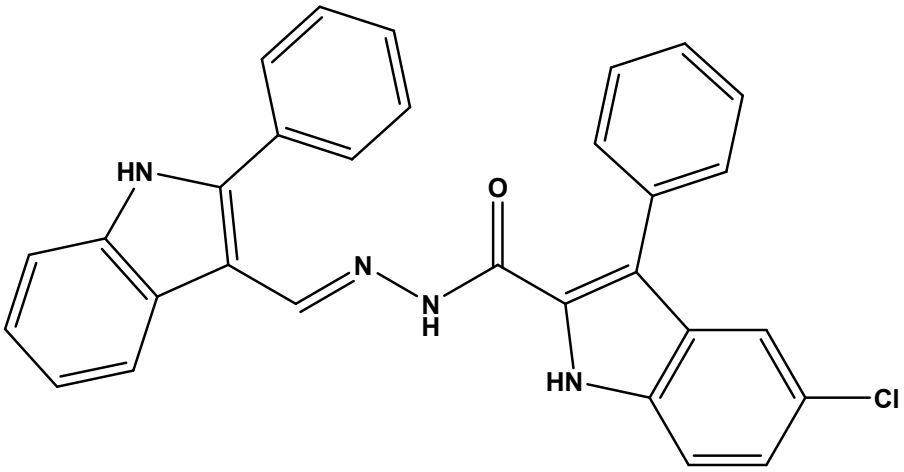


7c



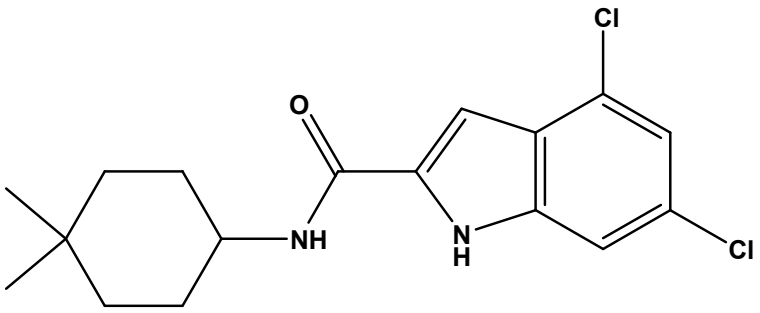
7d

In order to test for their in vitro antimycobacterial efficacy, Walmik *et al*. produced a number of new N'-((2- phenyl-1H-indol-3-yl) methylene, substituted phenyl1H-indole-2-carbohydrazide derivatives. According to the antitubercular results, chlorine compounds were the most effective. **7e** (MIC = 0.2 g/mL) is a chemical compound. shown a strong growth-inhibitory activity against Mycobacterium tuberculosis H37Rv.

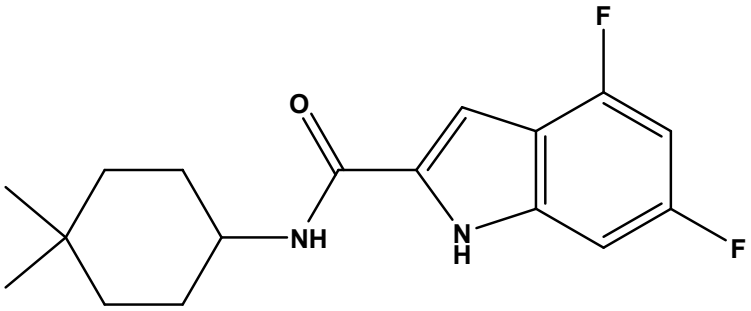


7e

According to Kondreddi *et al.,* N-(4, 4-dimethylcyclohexyl)-substitutedindole-2-carboxamides are effective against TB. Alkyl groups boosted activity and decreased solubility, according to structure-activity relationship (SAR) investigations on Mycobacterium TB. the **7f,** and **7g.**

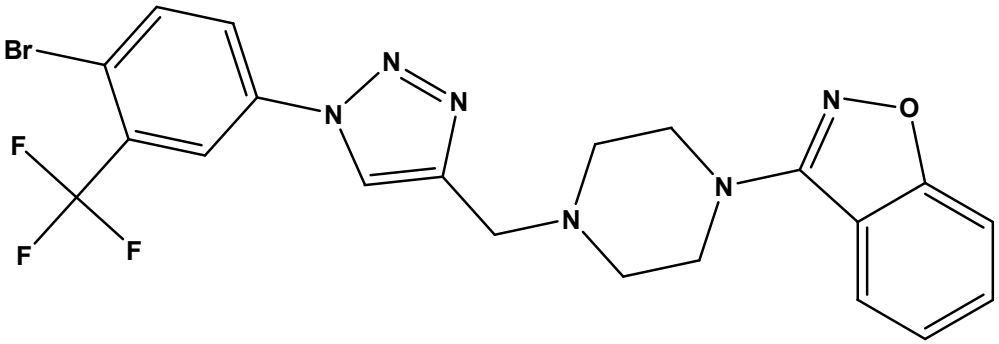


7f



7g

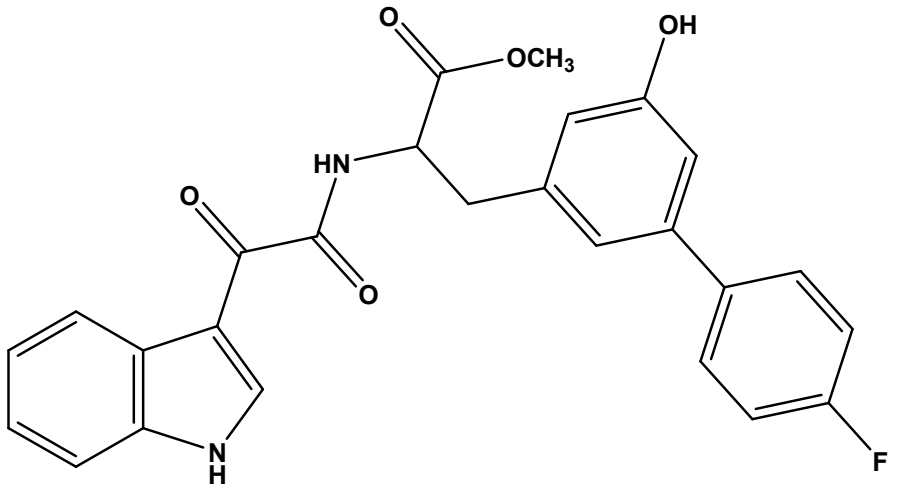
To combat the H37Rv strain of Mycobacterium tuberculosis, Naidu *et al.* developed different 3-(4-((1-(4-bromo3substitutedphenyl)-1H-1, 2, 3-triazol-4-yl) methyl) piperazin-1-yl) benzo[d]isoxazole derivatives. The studied chemical with the strongest antitubercular action was **7h** MIC = 6.16 M. The pantothenate synthetase enzyme was docked to study receptor interactions.



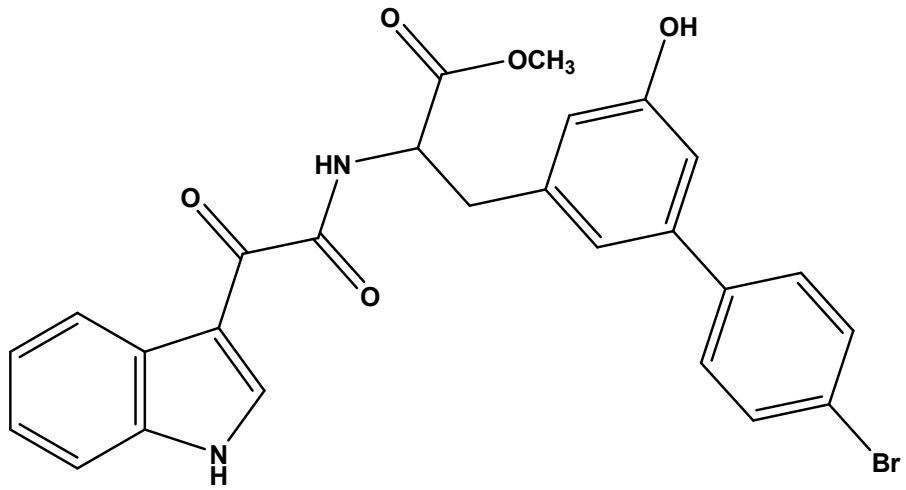
7h

Antimalarial

Vasconcelos et al. revealed the existence of derivatives of indole-3-glyoxyl tyrosine that are effective against the Plasmodium falciparum parasite. The antimalarial activity of **8a** and **8b**was good.



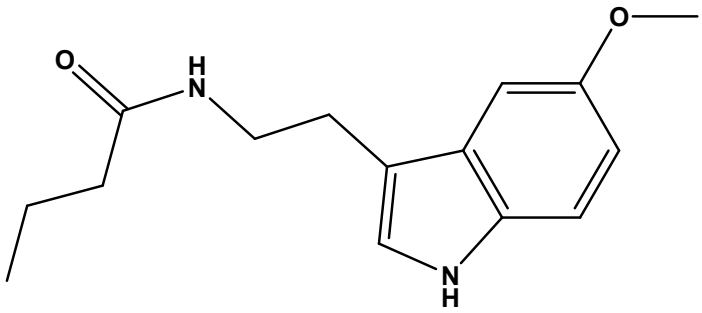
8a



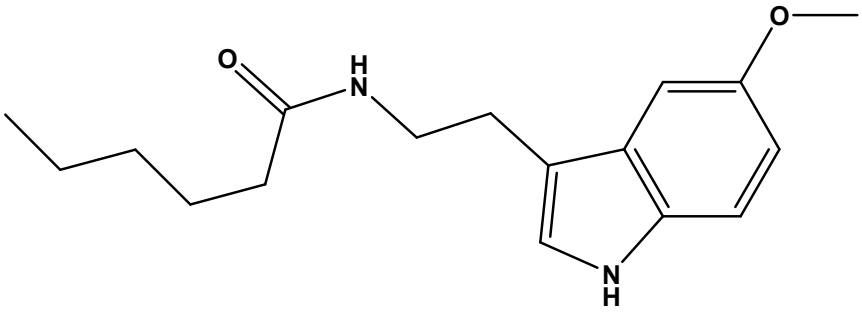
8b

In order to determine the antimalarial activity, Schuck *et al.* synthesised melatonin compounds and tested them in Plasmodium falciparum culture. The structural-activity relationship (SAR)

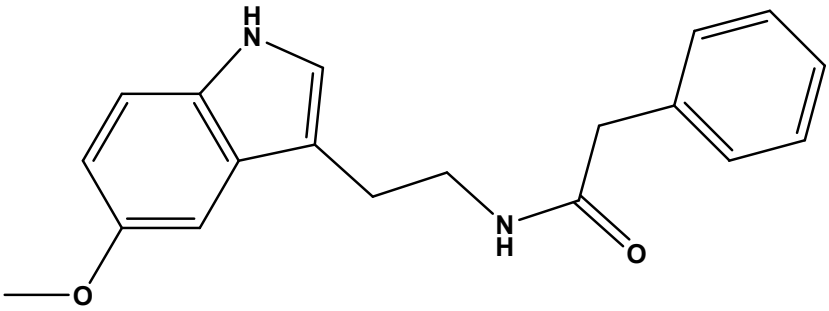
demonstrated that indole derivatives with carboxamide groups performed well. In low concentrations, the derivatives **8c, 8d** and **8e** were effective against Plasmodium falciparum



8c



8d



8e

III. CONCLUSION

There are several substances with different biological uses that include the indole molecule. An indole core is a component of the pharmacophore structure of many synthetic drug compounds,

and it aids in attaching pharmaceuticals to the residues of the binding site of targeted targets.Specifies the residues in the target molecules' intended binding sites.

The biological effects of derivatives with an indole core include antidiabetic, anticancer, antibacterial, anti-HIV, antiviral, anti-inflammatory, antioxidant, anticholinesterase, antitubercular, and antimalarial properties. These initiatives have made indole a focus of study for the identification of new chemical entities. These chemical compounds could make for safer and more potent medications for a variety of illnesses. Using the literature findings mentioned above as a summary, we can state that indole exhibits a wide range of biological activities. There is a great deal of room for further research on indole's potential as a novel treatment. The chemistry of the indole derivatives discussed in this study will aid scientists all around the world in the design and synthesis of innovative pharmaceuticals that will be helpful in the mitigation of a variety of illnesses.

REFERENCES

1. Cameron H. M. Zheng, Daria A. Balatsky, Rebecca C. DiPucchio, Laurel L. Schafer. The Catalytic Synthesis of N-Aryl Indoles Featuring an Alternative Disconnection. Hydroaminoalkylation for a Telescoped Reaction Sequence. *Organic Letters* 2022; *24* (36): 6571-6575.
2. Rishi R. Sapkota, Raj Kumar Tak, Vivek Aryal, Doleshwar Niroula, Nicholas C. Secosky, Roshan K. Dhungana, Ramesh Giri. Cu-Catalyzed Cyclization/Coupling of Alkenyl Aldimines with Arylzinc Reagents: Access to Indole-3-diarylmethanes. *Organic Letters* 2022; *24* (33): 6213-6218.
3. Haidong Liu, Renyi Xing, Kewei Ren, Fei Xue, Chao Feng. α-Iminyl Cation-Involved Indole Construction via Brønsted Acid-Promoted Reaction of Isoxazol-5-ones. *The Journal of Organic Chemistry* 2022; *87* (16) : 11226-11230.
4. Jie Huang, Ling-Ling Chen, Zhi-Min Chen. Palladium-Catalyzed Three-Component Cross-Coupling of Conjugated Dienes with Indoles Using Ethynylbenziodazolones as Electrophilic Alkynylating Reagents. *Organic Letters* 2022; *24* (31): 5777-5781.
5. Yue Dong, Xiangmin Li, Peng Ji, Feng Gao, Xiang Meng, Wei Wang. Synthesis of C-1 Deuterated 3-Formylindoles by Organophotoredox Catalyzed Direct Formylation of Indoles with Deuterated Glyoxylic Acid. *Organic Letters* 2022L; *24* (28): 5034-5039.
6. Nikita Kvasovs, Vladimir Gevorgyan. Accessing Illusive E Isomers of α-Ester Hydrazones via Visible-Light-Induced Pd-Catalyzed Heck-Type Alkylation. *Organic Letters* 2022; *24* (23): 4176-4181.

7. Lakhdar S, Westermaier M, Terrier F, Goumont R, Boubaker T, Ofial AR, Mayr H Nucleophilic reactivities of indoles. J Org Chem. 2006; 71:9088–9095
8. Sharma V, Pradeep K, Devender P. Biological importance of the indole nucleus in recent years: a comprehensive review. J Heterocycl Chem 2010; 47:491–502
9. Kaushik NK, Kaushik N, Attri P, Kumar N, Kim CH, Verma AK, Choi EH. Biomedical Importance of Indoles. Molecules 2013; 18:6620–6662
10. Xue S, Ma L, Gao R, Lin Y, Linn Z Synthesis and antiviral activity of some novel indole-2-carboxylate derivatives. Acta Pharmaceutica Sinica B 2014;4(4):313–321
11. Cihan-Üstündag G, Gürsoy E, Naesens L, Ulusoy-Güzeldemirci N, Çapan G Synthesis and antiviral properties of novel indole-based thiosemicarbazides and 4-thiazolidinones. Bioorg Med Chem 2016; 24:240–246
12. Sellitto G, Faruolo A, Caprariis PD, Altamura S, Paonessa G, Ciliberto G. Synthesis and anti-hepatitis C virus activity of novel ethyl1H-indole-3- carboxylates in vitro. Bioorg Med Chem 2010; 18:6143–6148
13. Tichy M, Pohl R, Xu HY, Chen YL, Yokokawa F, Shi PY, Hocek M.Synthesis and antiviral activity of 4, 6-disubstituted pyrimido[4,5-b]indole ribonucleosides. Bioorgan Med Chem, 2012; 20:6123–6133
14. Abdel-gawad H, Mohamed HA, Dawood KM, Badria FAR. Synthesis and antiviral activity of new indole-based heterocycles. Chem Pharm Bull 2010; 58(11):1529–1531
15. Sarva S, Harinah JS, Sthanikam SP, Ethiraj S, Vaithiyalingam M, Cirandur SR. Synthesis, antibacterial and anti-inflammatory activity of bis(indolyl)methanes. Chinese Chem Lett 2016; 27:16–20
16. Pedada SR, Yarla NS, Tambade PJ, Dhananjaya BL, Bishayee A, Arunasree KM, Philip GH, Dharmapuri G, Aliev G, Putta S, Rangaiah G. Synthesis of new secretory phospholipase A2-inhibitory indole containing isoxazole derivatives as anti-inflammatory and anticancer agents. Eur J Med Chem 2016;112:289–297
17. Chavan RS, More HN, Bhosale AV, Synthesis, characterization and evaluation of analgesic and anti-inflammatory activities of some novel indoles. Trop J Pharmaceutical Res 2011; 10(4):463–473
18. Shaker AM, Abdelall EK, Abdellatif KR, Abdel-Rahman HM. Design, synthesis and biological evaluation of 2-(4-(methylsulfonyl) phenyl) indole derivatives with promising COX-2 inhibitory activity. J Appl Pharm Sci. 2018; 8(11): 001–008
19. Zhuang SH, Lin YC, Chou LC, Hsu MH, Lin HY, Huang CH, Lien JC, Kuo SC, Huang LJ. Synthesis and anticancer activi ty of 2, 4-disubstituted furo[3,2-b]indole derivatives. Eur J Med Chem 2021; 66:466–479
20. Kasralikar HM, Jadhavar SC, Bhusare SR, Synthesis and molecular docking studies of oxochromenyl xanthenone and indolyl xanthenone derivatives as anti-HIV-1 RT inhibitors. Bioorg Med Chem Lett 2022; 25:3882–3886

21. Ran JQ, Huang N, Xu H, Yang LM, Lv M, Zheng YT. Anti HIV-1 agents 5: Synthesis and anti-HIV-1 activity of some N-arylsulfonyl-3-acetylindoles invitro. Bioorg Med Chem Lett 2022; 20:3534–3536
22. Ashok P, Lu CL, Chander S, Zheng YT, Murugesan S, Design, synthesis, and biological evaluation of 1-(thiophen-2-yl)-9H-pyrido [3, 4-b] indole derivatives as anti-HIV-1 agents. Chem Biol Drug Des 2019; 85(6):722–728
23. Ragno R, Coluccia A, La Regina G, De Martino G, Piscitelli F, Lavecchia A, Novellino E, Bergamini A, Ciaprini C, Sinistro A, Maga G. Design, molecular modeling, synthesis, and anti-HIV-1 activity of new indolyl aryl sulfones. Novel derivatives of the indole-2-carboxamide. J Med Chem 2021; 49(11):3172–3184
24. Silveira CC, Mendes SR, Soares JR, Victoria FN, Martinez DM, Savegnago L. Synthesis and antioxidant activity of new C-3 sulfenyl indoles. Tetrahedron Lett 2020; 54:4926–4929
25. Estevao MS, Carvalho LC, Ribeiro D, Couto D, Freitas M, Gomes A, Ferreira LM, Fernandes B, Marques MMB. Antioxidant activity of unexplored indole derivatives: Synthesis and screening. Eur J Med Chem 2021; 45:4869–4878
26. Suzen S, Tekiner-Gulbas B, Shirinzadeh H, Uslu D, Gurer-Orhan H, Gumustas M, Ozkan SA. Antioxidant activity of indole-based melatonin analogues in erythrocytes and their voltammetric characterization. J Enzyme Inhib Med Chem 2018; 28(6):1143–1155
27. Dixit A, Pathak D, Sharma GK. Synthesis, antibacterial and free radical scavenging activity of some newer N-((10-nitro-1H-indolo [1, 2-c] quinazolin12-yl) methylene) benzenamines. Eur Pharmaceutical J 1 2022; (ahead-of-print)
28. Ozturk A, Abdullah M. Toxicological effect of indole and its azo dye derivatives on some microorganisms under aerobic conditions. Sci Total Environ 2019; 358:137–142
29. Scribner A, Moore JA III, Ouvry G, Fisher M, Wyvratt M, Leavitt P, Liberator P, Gurnett A, Brown C, Mathew J, Thompson D, Schmatz D, Biftu T.Synthesis and biological activity of anticoccidial agents: 2,3-diarylindoles. Bioorg Med Chem Lett 2019; 19:1517–1521
30. Singh P, Verma P, Yadav B, Komath SS. Synthesis and evaluation ofindole-based new scaffolds for antimicrobial activities and Identification of promising candidates. Bioorg Med Chem Lett 2018; 21:3367–3372
31. Desai NC, Somani H, Trivedi A, Bhatt K, Nawale L, Khedkar VM, Jha PC, Sarkar D. Synthesis, biological evaluation and molecular docking study of some novel indole and pyridine based 1, 3, 4-oxadiazole derivatives as potential antitubercular agents. Bioorg Med Chem Lett 2016; 26:1776–1783.
32. Walmik P, Saundane AR. Synthesis of novel indolyl-azetidinone and thiazolidinone derivatives as a potent antioxidant, antimicrobial and antitubercular agents. Der Pharma Chemica 2017; 6(4):70–79
33. Kondreddi RR, Jiricek J, Rao SP, Lakshminarayana SB, Camacho LR, Rao R, Herve M, Bifani P, Ma NL, Kuhen K, Goh A, Chatterjee AK, Dick T, Diagana TT, Manjunatha

UN, Smith PW. Design, synthesis, and biological evaluation of indole-2-carboxamides: a promising class of antituberculosis agents. J Med Chem 2017; 56(21):8849–8859

34. Naidu KM, Srinivasarao S, Agnieszka N, Ewa AK, Kumar MMK, Sekhar KVGC. Seeking potent anti-tubercular agents: Design, synthesis, antitubercular activity and docking study of various ((triazoles/indole)-piperazin1-yl/1, 4-diazepan-1-yl) benzo [d] isoxazole derivatives. Bioorg Med Chem Lett 2016; 26(9):2245–2250
35. Vasconcelos SN, Meissner KA, Ferraz WR, Trossini GH, Wrenger C, Stefani HA. Indole-3-glyoxyl tyrosine: synthesis and antimalarial activity against Plasmodium falciparum. Future Med Chem 2019; 11(6):525–538
36. Schuck DC, Jordão AK, Nakabashi M, Cunha AC, Ferreira VF, Garcia CR. Synthetic indole and melatonin derivatives exhibit antimalarial activity on the cell cycle of the human malaria parasite Plasmodium falciparum. Eur J Med Chem 2019; 78:375–382