Chemistry Research Journal, 2021, 6(4):17-30

Available online www.chemrj.org

Review Article

ISSN: 2455-8990
CODEN(USA): CRJHA5

Indole: A Versatile Heterocyclic

Shalini*, Surendra Kumar Gautam, Shobhit Srivastava, Sujeet Kumar Gupta

*Department of Pharmaceutical Chemistry, Hygia Institute of Pharmaceutical Educational and Research, Lucknow, India, 226021.
Email id: shalini202183@gmail.com

Abstract Indole is a heterocyclic compound comprise of benzene and pyrrole ring. The Indole nucleus plays an important role in medicinal chemistry to synthesized a series of multiple biological active derivatives such as Anti-inflammatory, Anti-proliferative, Anti-bacterial, Antidiabetic, Antioxidant, Antifungal, Anticancer etc. Various indole derivatives and substituents are mention in article. These derivative of carbazole are tested for varying pharmacological activities. The main motive of the review article to describe their pharmacological action and activities against different type of bacteria using different type of models (*in vitro* assay, *in vivo* assay etc). Different methods for synthesizing Indole derivatives and pharmacological action are discussed.

Keywords Indole, Synthesis, Biological activity

1. Introduction

Indole was found by Adolph Baeyer as an out-development of his popular examinations on the constitution of indigo. Throughout his examination of indigo, Baeyer had available to him two indigo subordinates isatin, its oxidation item and indigo white, its decrease item. Isatin had been known since 1841 [1].

The structure of indole was at long last affirmed by Baeyer and his understudy Emmerling. The substance by the combination of *o*-nitrocinnamic corrosive with iron filings and soluble base; the decrease of the nitro gathering and ring conclusion to indole came about. From this response, the thought of Kekule's new benzene structure hypothesis, Baeyer doled out it the benzopyrrole structure which before long came into general acknowledgment [2-3].

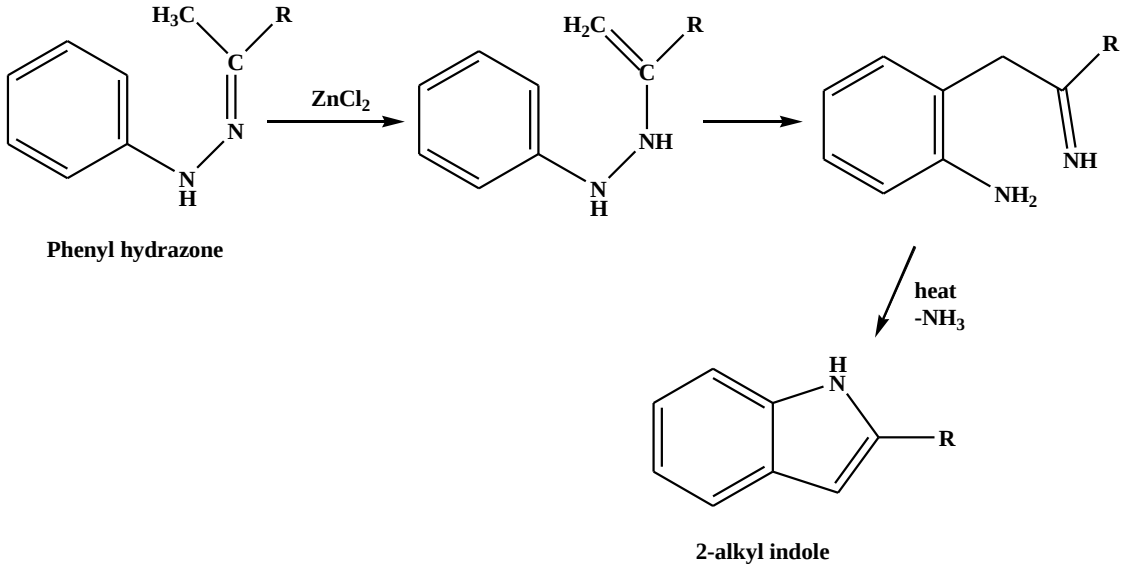
The indole ring system is probably the most ubiquitous heterocyclic in nature. Owing to the great structural diversity of biologically active indoles, it is not surprising that the indole ring system has become an important structural component in many pharmaceutical agents [4-5]. Substituted indoles have been referred to as confidential structures since they are capable of binding to many receptors with high affinity [6]. Overall one hundred years, the synthesis and functionalization of indoles have been a major area of focus for synthetic organic chemists, and numerous methods for the preparation of indoles have been developed. In some cases, specific substitution patterns remain difficult to obtain by the standard indole-foaming reaction; thus new methodologies emerge [7].

Indole chemistry begins to develop with the study of the dye indigo. The word Indole is a coin from the word India, a blue dye imported from India known as Indigo. The name indole is a blend of the words indigo and oleum since indole was first isolated by treatment of the indigo dye with oleum. Indole is a benzopyrrole in which the benzene and pyrrole rings are fused at the 2-and 3-positions of the pyrrole nucleus. The Indole nucleus has ten π- electrons which are circulating over nine atoms. So, Indole is electron rich system. Its resonance energy is 47-49 Kcal/mole. The electrons on nitrogen are involved in aromatic sextet; hence it is a very weak base with pK_a value -3.5 [8-9].

Principally, indole was extracted from coal tar and first obtained by Adolf Baeyer by the pyrolysis of oxindole with zinc dust in 1886. Oxindole was obtained from the reduction of isatin was obtained from oxidizing the natural insoluble dark blue dye called indigo. Indole is made up of a benzene ring, fused with a pyrrole ring. It occurs in coal-tar, orange blossoms, jasmine flowers and jonquil extracts [10-11].

2. Synthesis

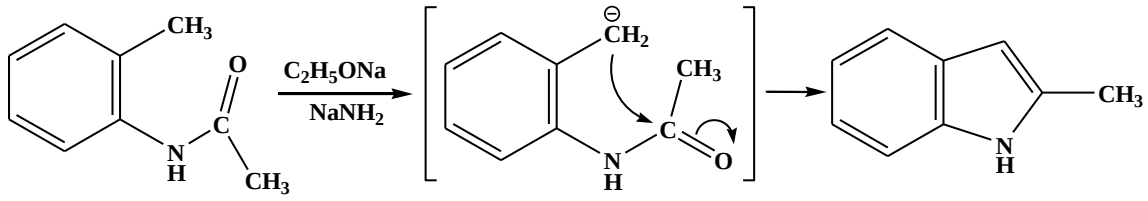
Fischer indole synthesis was named after the chemist Fischer in 1866. It is the most important method for the preparation of indole. In this method, phenylhydrazone or substituted phenylhydrazone of an aldehyde or ketone or ketonic acid is heated in the presence of the catalyst as $ZnCl_2$, BF_3 etc [12].



Phenyl hydrazone

2-alkyl indole

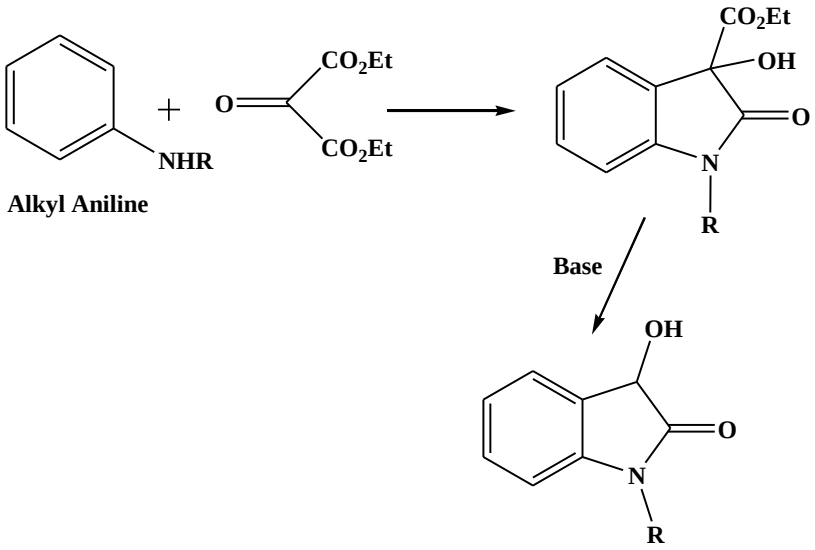
This method was first reported by Madelung synthesis in 1912. The cyclization of N-*o*-alkyl anilines is accomplished. Thus the amide *o*-methyl acetanilide with a strong base at elevated temperatures gives 2-methylindole. The reaction is heated in the presence of a base (C_2H_5ONa, $NaNH_2$, etc.) and in the absence of air.



***O*-methyl acetanilide**

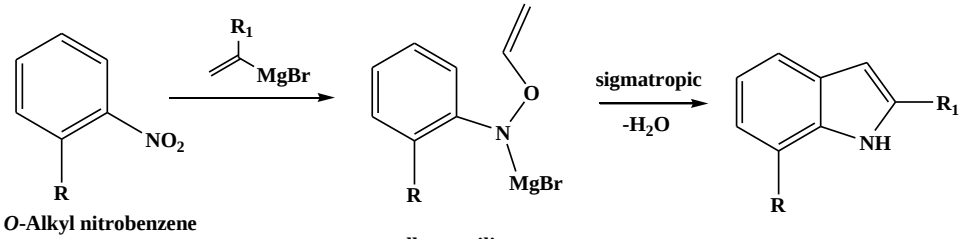
2-Methylindole

In this chemical reaction an alkyl amine or primary or secondary aniline is condensed with ethyl or methyl ester of mesoxalic acid to make a dioxindole martinet synthesis. It was established in 1913 by J. Martinet.



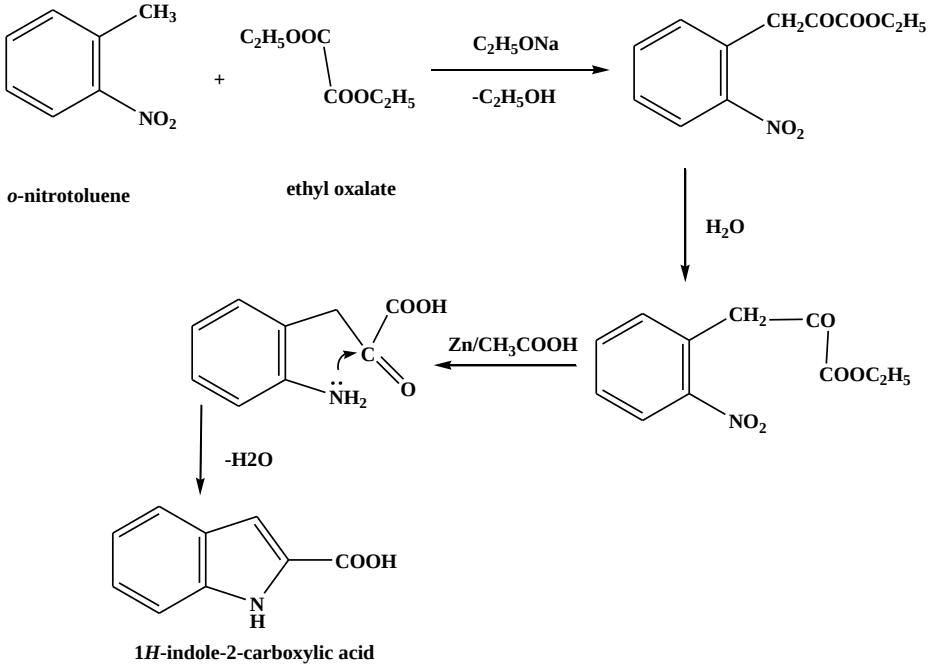
Alkyl Aniline

In Bartoli indole synthesis (1978) substituted indoles are obtained by the reaction of ortho-substituted nitroarenes with vinyl Grignard reagents. In absence of ortho substitution on nitroarene, reaction fails [13].



***O*-Alkyl nitrobenzene** **alkoxyaniline**

In this method, it is the base catalysed intermolecular cyclization of phenylpyruvic acid derivatives. It was given by Reissert synthesis in 1897. In this reaction *o*-nitro toluene undergoes Claisen condensation with oxalic ester in the presence of strong base (C_2H_5ONa) to yield the pyruvic ester. As this is reduced with Zn/CH_3COOH, to gives corresponding indole-2-carboxylic acid.



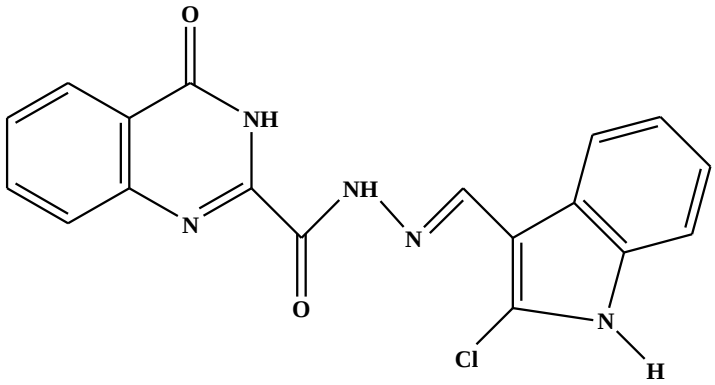
***o*-nitrotoluene** **ethyl oxalate**

1*H*-indole-2-carboxylic acid

3. Biological Activity

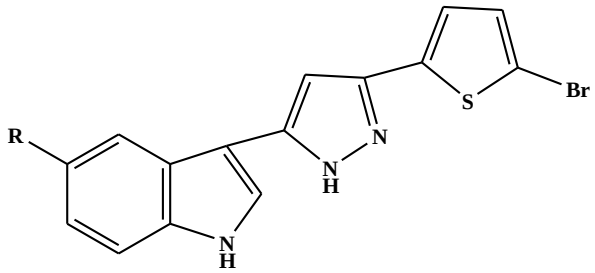
Anti-Microbial Activity

Li *et al.* 2018 a series of novel quinazolinone acyl hydrazone derivatives containing the indole moiety were synthesized and evaluated compound **1a** for their inhibition activities against three phytopathogens fungi named *Pellicullariasasakii (P. sasakii), Verticillium dahlia (V. dahlia),* and *Phytophthora infestans (P. infestans)* were first evaluated at *in vitro* based on the turbidimetric method. Antibacterial experiments indicated two compounds exhibited remarkable inhibition activities against tested bacteria [11].

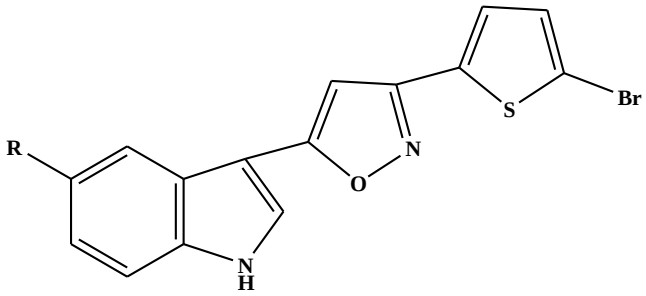


(1a)

Reddy *et al.* 2017 A new class of 3,5-disubstituted pyrazoles and isoxazoles were prepared from the Michael acceptors 1-furanyl / thiophenyl / pyridinyl-3-indole-prop-2-en-1-ones under ultrasonication and evaluated for antimicrobial activity. Amongst all the tested compounds fluoro substituted thiophene linked **$1a_1$**and **$1b_1$** compounds displayed promising antibacterial activity particularly against *Bacillus subtilis* and antifungal activity against *Aspergillus niger*. Also, compounds with more number of electron withdrawing groups showed higher antimicrobial activity [14].

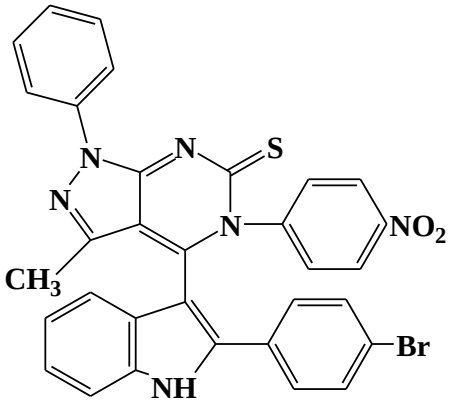


($1a_1$) R=a) H; b) F



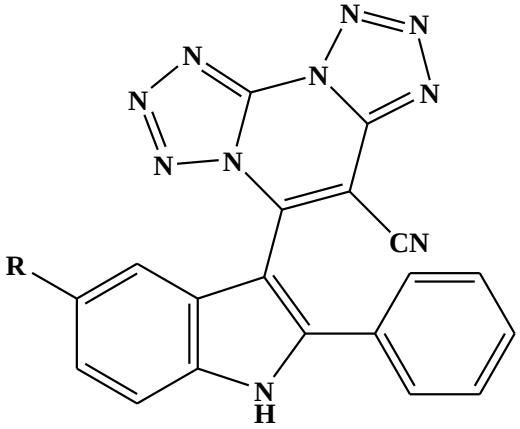
($1b_1$) R= a) H; b) F

Salman *et al*. 2015 reported by synthesized reaction of indole-3-carboxaldehydes with hydrazine derivatives and different substituted acid hydrazides hydrazine derivatives and acid hydrazide derivatives. Screening for some selected compounds was carried for their potential antibacterial, antifungal activity. Most of the tested compound betters activity against the Gram-positive and Gram negative bacteria. Compounds **$1a_2$, $1b_2$ and $1c_2$** exhibited excellent activity against *Staphylococcus aureus*, *Bacillus subtilis* and *Escherichia coli* compared with the standards drugs, while compounds **$1c_2$** have strong antifungal activity against *Aspergillus fumigatus* and *Candida albicans* comparable to *Amphotericin* B [15].



($1c_2$)

Raghunath *et al.* 2011 a new series of tetrahydropyrimidines, pyrazolopyrimidines and ditetrazolopyrimidines were compound **(1a3-c3)** synthesized. The newly synthesized compounds have been tested for their antimicrobial and antioxidant activities against DPPH stable free radical. In the case of antibacterial activity, compounds **1a3** and **1c3** exhibited the maximum zone of inhibition against *Staphylococcus aureus*, compound **1c3** more potent exhibited maximum zone of inhibition against *Pseudomonas aeruginosa* [16].

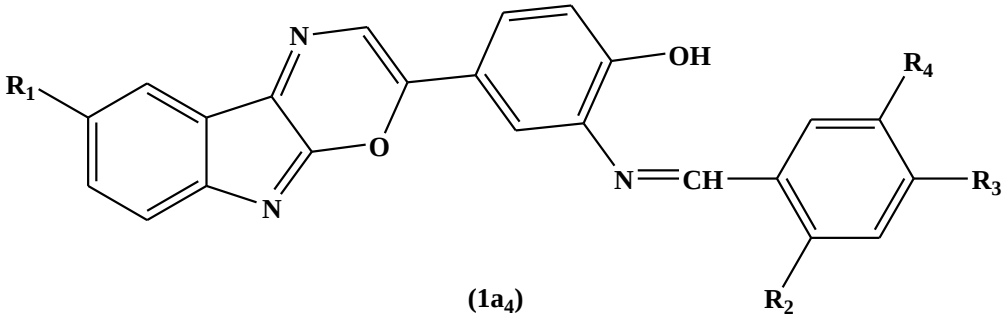


($1a_3$-c_3)

Compound	**$1a_3$**	**$1b_3$**	**$1c_3$**
R	Cl	CH_3	H

Nataraj *et al.* 2010 The series of indole-2,3-diones was prepared and condense with 3-amino-4-hydroxy benzoic acid hydrazide. The compound **$1a_4$** have been synthesized by the cyclization of 3-amino-4-hydroxy-benzoic acid (2-oxo-1, 2-dihydro-indol-3-ylidene)-hydrazide in presence of concentrated H_2SO_4 to gives 2-{(benzalamino-4-hydroxybenzyl) (1, 3, 4)-oxadiazino [6, 5-b]} indole indicated the compound exhibits a marginal antibacterial

activity against *Bacillus subtilis, Staphylococcus aureus* and fungal activity compound were performed by against *A. Niger, C. verticulata* CUP-plate method [17].

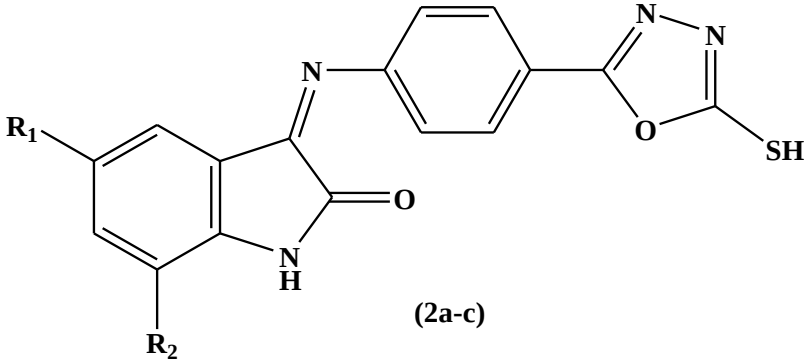


($1a_4$)

Compound	R_1	R_2	R_3	R_4
$1a_4$	H, Br, NO_2	H, OH	H, OH, OCH_3	H, OCH_3

Anti-Cancer Activity

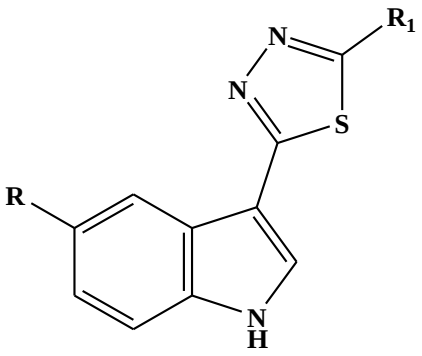
Gudipati *et al.* 2011 reported a series of 5- or 7-substituted 3-{4-(5-mercapto-1, 3, 4-oxadiazol-2-yl) phenylimino}-indolin-2-one derivatives were synthesized by treating 5-(4-aminophenyl)-1, 3, 4-oxadiazole-2-thiol with different isatin derivatives. All the synthesized derivatives were screening for *In vitro* anticancer activity against HeLa, IMR-32 & MCF-7 cancer cell lines using MTT method. The synthetic compounds produced a dose dependant inhibition of growth of the cells. The synthesized compound, 5-halo substituted compounds **(2a-c)** was found to most potent anticancer agents [18].



(2a-c)

Compound	2a	2b	2c
R_1	F	Cl	Br
R_2	H	H	H

Kumar *et al.* 2010 has synthesized a novel series of 5-(3-indolyl)-2-substituted-1, 3, 4-thiadiazoles **($2a_1$-m_1)** were the performed reaction of indole-3-carboxylic acid with aryl hydrazides *N, N'*diacylhydrazines the treatment with Lawson's reagent resulted in the formation of the indoly-1, 3, 4-thiadiazoles.The synthesized compoundwere screened against prostate (PC3, DU145 and LnCaP), breast cancer (MCF7 and MDA-MB-231) and pancreatic ($PaCa_2$) cancer cell lines. The Compound **$2m_1$** with 4-benzyloxy-3methoxyphenyl and 5-bromo indolyl substituted is the most potent compound cancer cell line [19].

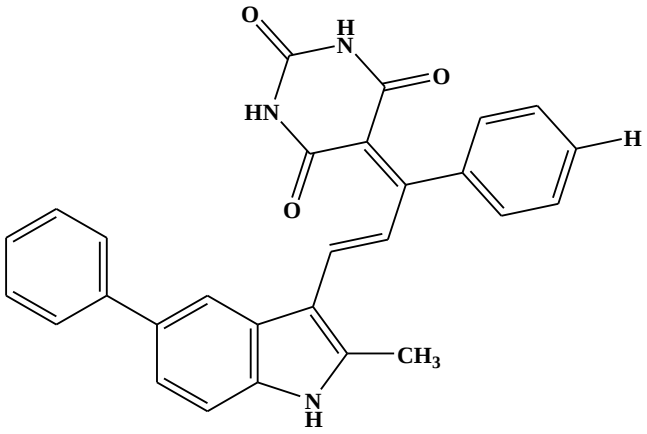


($2m_1$)

R=Br**; R1=** 4-BnO-3-$OCH_3C_6H_3$

Anti-oxidant Activity

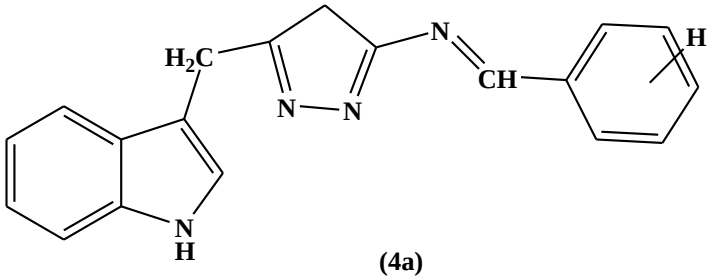
Birader *et al.* 2010 a newly series of novel indole derivatives containing barbitone moiety **(3a-i)** were synthesized by condensation of chalcones and barbituric acid. The synthesis compounds are screened for antioxidant and DNA cleavage activities evaluated. The simple indole derivatives compound **3a, 3d** and **3g** were as concluded potent derivatives and **3b** shows excellent antioxidant activity by DPPH method [20].



(3b)

Cardiovascular Activity

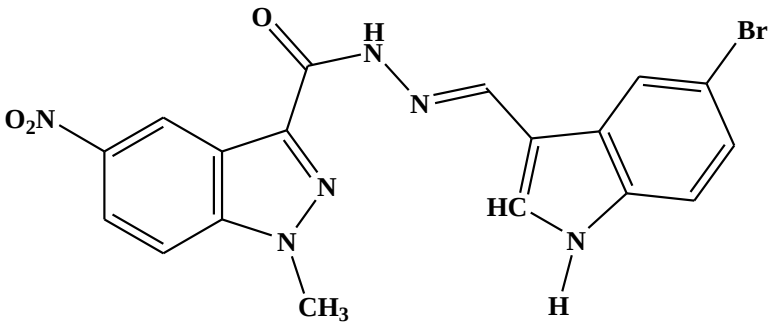
Singh *et al.* 2013 reported a series of substituted indole derivatives containing the oxadiazole and thiazolidinones side chain at 3- position and screened for their cardiovascular activity by observing the effect on blood pressure, heart rate and pressor responses evoked either by carotid occlusion (CO) or intravenous noradrenaline in albino rats. A compound **4a** of the synthesized series having thiazolidinones side chain was found most potent and associated with inhibition of CO response without affecting NA response [21].



(4a)

Anti- Tumor Activity

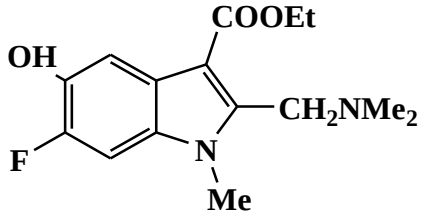
Sreenivasulu *et al.* 2017 has discovered by synthesis of novel hydrazide–hydrazones linked between indole and indazole moieties **5a-h.** All the synthesized derivatives were evaluated for their anticancer activity against human cancer cell lines (HeLa, MDA-MB-231, MCF-7, and A549). The synthesis was observed that three compounds **5a, 5b** and **5c** promising cytotoxicity on different cell lines. Compound **5c** cytotoxic effect on HeLa and A549 cancer cell lines with IC_{50} values of 6.86 and 7.9µM. The removal of the *N*-methyl group from bromoindole ring gave the compound **5c** which was the most potent analogue and was identified as a promising lead drug. The compounds were observed to the selective inhibition against breast cancer cell lines [22].



(5c)

Anti-Viral Activity

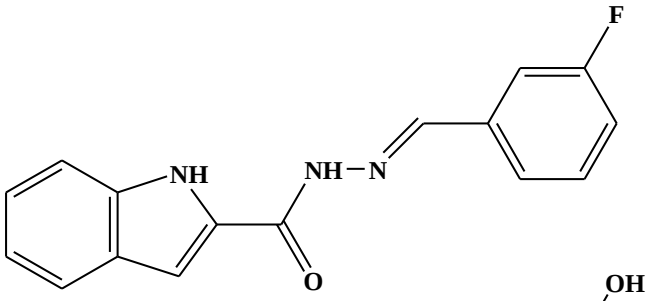
Ivachtchenko *et al.* 2015 a novel series of 2-aminomethyl-5-hydroxyl-1*H*-indole-3-carboxylic acid were synthesized and derivatives **6d.**Arbidol, generally had low potential hepatotoxicity (CC_{50}). The antiviral activity showed that the compounds synthesized inactive against was investigated to bovine virus, diarrhea virus, heapetits C and influenza virus. The antiviral activity is the compound synthesized by bovine virus diarrhea virus (BVDV) and led weak in relation to human hepatoma cell line Hub 7.3 with sensitivity to HCV infection. Compound **6c** and **6d** were then compared with Arbidol in a mouse influenza pneumonia model using animals infected with A/Aichi/2/69 (H3N2) virus in MDCK cell cultures. The compound **6d** more active and having a larger therapeutic index than 6c compound [23]**.**



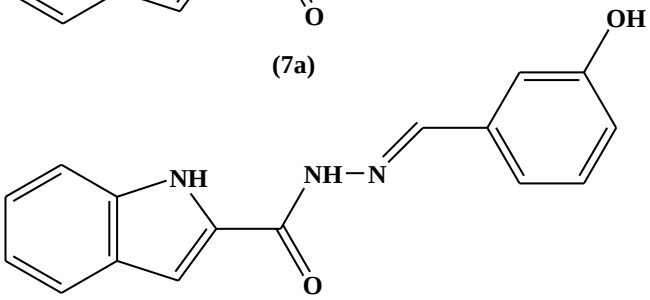
(6d)

Anti-Platelet Activity

A series of *N*-substituted indole carbohydrazine derivative was reported by Mirfazli *et al*. 2014. The indole derivative was synthesized by hydrozinolysis of methyl 1*H*-indole-3-carboxylate followed by condensation of obtained hydrazine intermediate. The reported compound **7a** and **7b** was found most potent when the synthesized series was screened for their anti-platelet aggregation activity induced by arachidonic acid, adenosine diphosphate and collagen in fresh human blood [24].



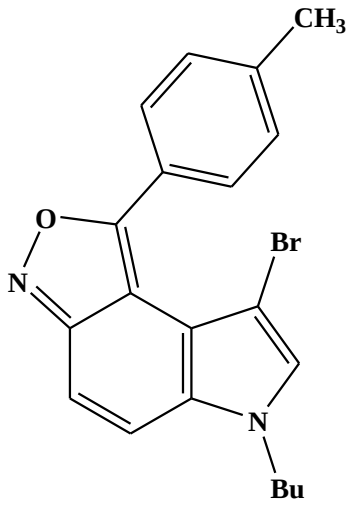
(7a)



(7b)

Anti-Bacterial Activity

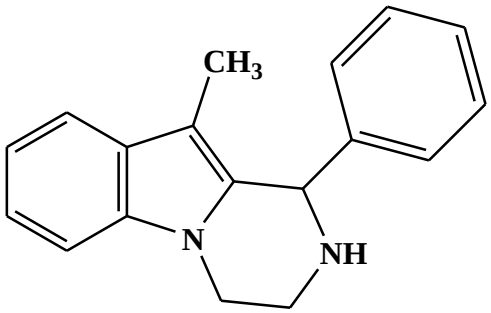
Pordel *et al.* 2013 discovered by a new synthesize compounds 8-bromo-6-alkyl-1-aryl-6*H*-isoxazolo [4, 3-e] indole derivatives (**8a**–**h**) were starting 3-bromo-1-alkyl-5-nitro-1*H*-indoles prepared by 5-nitro-1*H*-indole with bromine in the presence of DMF. All the newly synthesized compounds were screened for their antibacterial activity against gram positive bacteria, *Escherichia coli* (HB101), *Staphylococcus aureus* pathogens (methicillin resistant *S. aureus* an methicillin susceptible *S. aureus), Pseudomonas aeruginosa*, and *Bacillus subtilis*. The MIC values of these compounds were determined. The compounds were found to be **8g** the best inhibitory activity against antibacterial activity [25].



(8g)

Tiwari RK *et al.* 2006 has reported a novel synthesize of substituted 1, 2, 3, 4-tetrahydrazino-[1,2a] indole derivatives **($8a_1$-f_1)** .The compound 2-(3-methyl-1*H*-indolyl-1) ethylamine was obtained by the reaction of 3-methylindole with 2-choloroethylamine. The intermediate 2-(1*H*-1, 2, 3, 4-benzotriazol-1-ylmethyl)-10-methyl-1, 2, 3, 4-tetrahydropyrazino [1, 2-a] indole screened were synthesized and against positive bacteria and negative bacteria strains of namely *Staphylococcus aureus* (MTCCB 737). The synthesized compounds were mediate activity. The

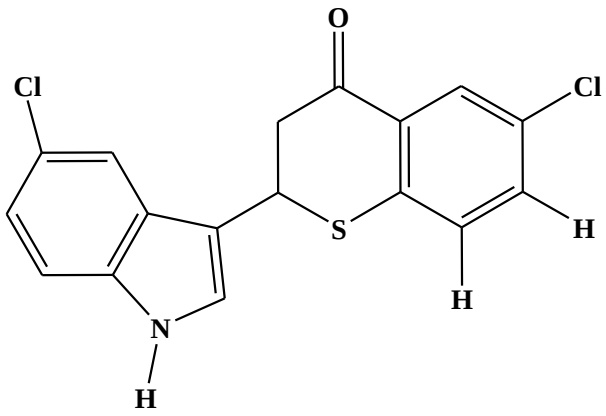
compound **$8a_1$** were most potent activity against pathogenic bacteria. *In vitro* antibacterial activity was tested by disc diffusion method using pathogenic strains of *Stalphylococcus aureus, S. typhi, P. aeruginosa and E.coli* [26].



($8a_1$)

Anti-fungal Activity

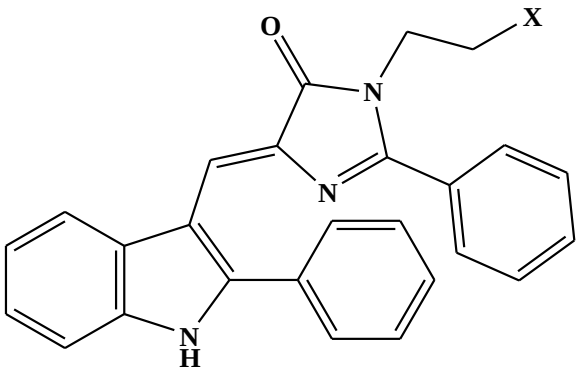
Song *et al.* 2015 discovered by a new series of 2-(indol-3-yl)-thiochroman-4-ones were synthesized by an ionic liquid catalyzed from thichromone and indole **(9a-o)**. These synthesized compounds were screened for antifungal activity against *Candida albicas, Mucor racemosa* by the serial plate dilution method. The compounds have best excellent inhibition than fungi .The best MIC values of compounds **9g, 9d** and **9h.** The compound was synthesizing **9d** most excellent inhibition of antifungal activity [27]**.**



(9d)

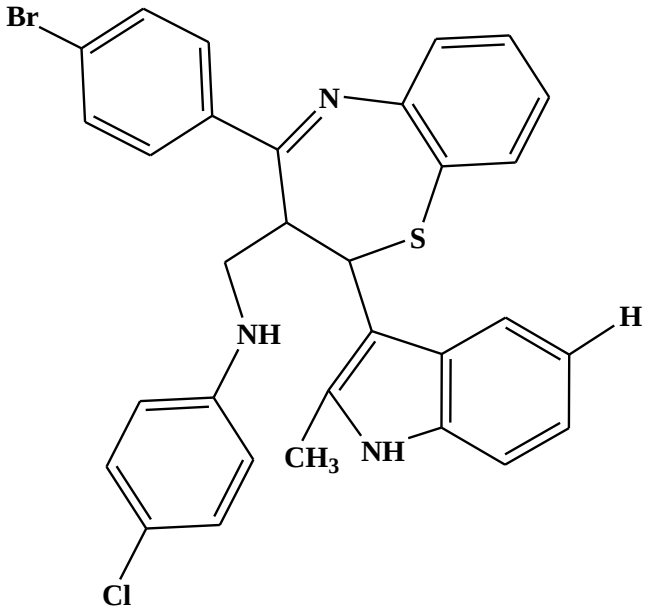
Anti-Convulsant Activity

Hussain *et al.* 2015 has reported a synthesized of indolyl-imidazolones was prepared 2-phenyl-1*H*-indole-3-carbaldehyde with benzoyl glycine in acetic anhydride in the presence of fused sodium acetate gave 2-phenyl-4-[(2-phenyl-indolin-3-yl)methylene)oxazol-5(4*H*)-one and 1,2,4-trisubstituted-1*H*-imidazol-5-(*4H)*-ones (**10a,b**). The synthesiszed compounds 10a and 10b were found to be highly active against MES test. Anticonvulsant activity of the compounds was determined in swiss albino mice by using MES and scPTZ animal models [28].



10a,10b= X= OH,NH_2

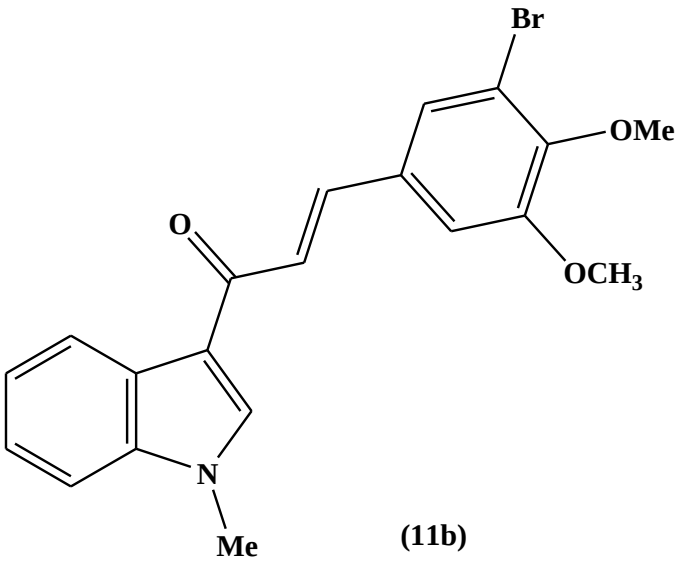
Kumar *et al.* 2011 reported by a series of 3-(4-substituted phenyl)-3-substituted phenyl aminomethylene)-2, 3-dihydrobenzoxapin-2-yl)-2, 5-disubstitiuted indoles starting from substituted phenyl chalconyl-2,5-disubstituted indoles were synthesized by the reaction of 4-chloro actophenone and substituted indole-3-carbaldehyde compound react with aniline and formaldehyde in the presence of methanol compound **$10a_1$**. The entire newly synthesized compound, screened compound was found to be most potent against anticonvulsant activity. The anticonvulsant activity was performed the method convulsiometer by using albino rats [29].



$10a_1$

Anti-proliferative Agent

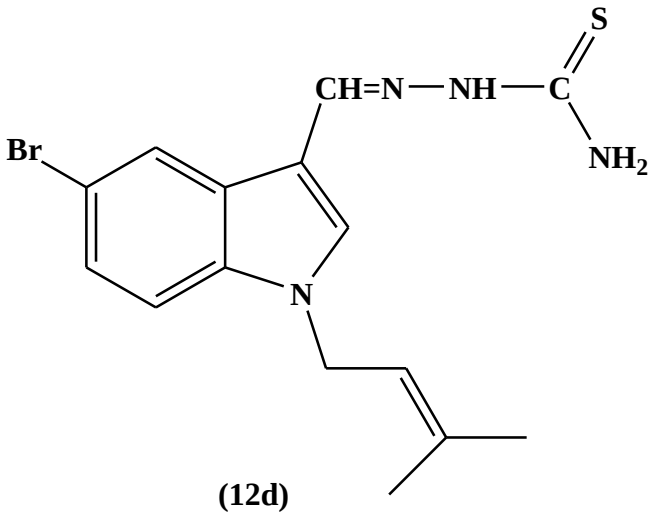
Mirzaei *et al.* 2017 discovered by the synthesized an indole-derived chalcones containing 3bromo-3,5-dialkoxylated phenyl moiety. The cytotoxic activities of synthesized compounds **(11a-k)** were evaluated against three human cell lines including adeno-carcinomic human alveolar epithelial cell (A549), breast cancer cells (MCF7) and human ovarian carcinoma cells (SKOV3) using MTT assay. The compound **11b** was more potent than etoposide against adenocarcinomic human alveolar basal epithelial cells (A549) [30].



(11b)

Cytotoxicity Activity

A series of novel N-1 and C-3 substituted indole derivatives were designed synthesized and evaluated for their cytotoxic properties by Choppra *et al.* 2015. The biological and pharmacological activities associated with indole and carbazone skeletons. The compound 1-(5-sybstituted-1-(3-methylbut-2-enyl)-1*H*-indole-3-yl)methylene) carbazides (**12a–f**). The compound **12c** and **12d** exhibits good cytotoxicity with LD_{50} of 6.49µM and its relative active was close at hand to podophyllotoxin. Inhibition of 5-LOX may lead to development of new therapeutic treatments for pathologies such as asthma. The compound **12d** more potent than unsubstituted analogues [31].



(12d)

4. Conclusion

The fused bicyclic indole moiety with one nitrogen atom at first position has emerged as a valuable scaffold in the medicinal chemistry and drug design. Not only the pharmacophoric features of core moiety, but substitution of different groups especially at various positions of ring resulted in development of potent compounds with antimalarial, anticancer, antileishmanial, anticonvulsion, antiviral antifungal and bacterial activities. Further efficient optimization of indole derivatives with multiple biological activities can lead to a potential poly-functional agents

for treatment of various diseases. In the future it is expected that research will reveal interesting aspects of indole as flexible moiety in order to develop a wide range of potent compounds.

References

[1]. Katritzky, A.R., (1985). *Handbook of Heterocyclic Chemistry*, Pergamon Press, New York. 47.

[2]. Kusama, H., Kurashige, M., Arakawa, H., (2005).*Journal of Photochemical and Photobiology* A: Chemistry, 16(9): 169–176.

[3]. Erdmann, A., *J. Praki. chem*., (1841). 24, 1.

[4]. Baeyer, A., Emmerling A., *Ber.*, (1869). 2: 679.

[5]. Sundberg, R.J., (1970). *The Chemistry of indoles*, Academic press, New York.

[6]. Eavans, B.E., Rittle, K.E., Bock, M.G., Dipardo, R.M. *et al.*, (1988). Methods for Drug Discovery: Development of Potent, Selective, Orally Effective Cholecystokinin Antagonists. *Medicinal Chemistry Research*, 31:2235-2246.

[7]. Gribble, G.W., (2000). *Journal Chemistry Society*, Perkin trans., Vol.1.

[8]. Sundberg, R.J., (1970). *The Chemistry of Indoles*, Academic Press, New York.

[9]. Baeyer, A., (1866). *Annual Medicinal Chemistry*, 140 (3): 295.

[10]. Pandeya, S.N., (2004). *A text book of pharmaceutical organic chemistry*, SG publishers, first edits. Reprinted, Vol. II, pp. 85-89.

[11]. Li, X.Q., Gan, Y.Y., and Meng, J., (2018). Synthesis and antimicrobial activities of novel quinazolinone, acylhydrazone derivatives containing the indole moiety, *Journal of Heterocyclic Chemistry*, 55(1):1382-1390.

[12]. Roussel, P. A. (1953). The Fischer indole synthesis. *Journal of Chemical Education*, *30*(3), 122.

[13]. Li, J. J. (2009). Bartoli indole synthesis. In *Name Reactions* (pp. 20-21). Springer, Berlin, Heidelberg.

[14]. Reddy, S.P., Yamini, G., Sowmya, D.V. (2017). Synthesis and antimicrobial activity of some new 3,5-disubsituted pyrazoles and isoxazoles, *Medicinal Chemistry*, 7(12): 371-380.

[15]. Salman, A.S., and Mahmoud, N.A., (2015). Synthesis, reactions and antimicrobial activity of some new 3-substituted indole derivatives, *International Journal of Organic Chemistry*, 5(2): 81-99.

[16]. Raghunath, S.A., Manjunatha, Y., (2012). Synthesis, antimicrobial and antioxidant activities of some new indole analogues containing pyrimidine and fused pyrimidine systems, *Medicinal Chemistry Res*, 21: 3809-3817.

[17]. Natraj, K.S., Rao, V.J., (2010). Synthesis and antimicrobial activity of new indole derivatives, *International Journal Chemistry Scienece*, 8(1): 609-616.

[18]. Gudipati, R., Anreddy, R.N.R., Manda. S., 2011. Synthesis, characterization and anticancer activity of certain 3-[4-(5-mercapto-1,3,4-oxadiazole-2 yl)phenylimino]indolin-2-one derivatives, *Saudi Pharmaceutical Journal*, 19(3): 153-158.

[19]. Kumar, D., Kumar, N.M., (2010). Synthesis and anticancer activity of 5-(3-indolyl)-1,3,4-thiadiazoles, *European Journal of Medicinal Chemistry*, 45(10): 4664-4668.

[20]. Biradar, J.S., Sasidhar, B.S., Parveen, R., (2010). Synthesis, antioxidant and DNA cleavage activites of novel indole derivatives, *European Journal of Medicinal Chemistry*, 45: 4074-4078.

[21]. Sing, N., Aggarwal, R.C., Sing, C.P., (2013). Cardiovascular activity of indole derivatives by incorporating oxadiazole, azetidinone and thiazolidinone moieties, *International Journal of Pharmaceutical Sciences and Drug Research*, Vol. 6(1): 14-17.

[22]. Sreenivasulu, R., Sujitha, P., Jadav, S.S., Ahsan, M.J., Kumar, C.G., (2017). Synthesis antitumor evaluation and molecular docking studies of indole indazolyl hydrazide hydrazine derivatives, *Monatsh chemistry*, 148(2): 305-314.

[23]. Ivachtchenko, A.V., Yamanushkin, P.M.., Mitkin, O.D., (2015). Synthesis and antiviral activity of substituted ethyl-2-aminomethyl-5-hydroxy-1*H*-indole-3-carboxylic acid and their derivatives, *Pharmaceutical Chemistry Journal*, 49(3): 151-162.

[24]. Mirfazli, S.S., Kobarfard, F., Firoozpour,L., Asdipour, A., Esfahanizadeh, M., Tabib, K., (2014). *N*-Substituted indole carbohydrazide derivatives: synthesis and evaluation of their antiplatlet aggregation activity, *DARU Journal of Pharmaceutical Sciences*, 22(1): 1-10.

[25]. Pordel, M., Abdollani, A., Razavi, B., (2013). Synthesis and biological evaluation of novel isoxazolo[4,3-e] indoles as antibacterial activity, *Russian Journal of Bioorganic Chemistry*, 39 (2)*:* 211-214.

[26]. Tiwari, R.K., Singh, D., (2006). Synthesis and antibacterial activity of substituted 1,2,3,4-tetrahydrozino(1,2a) indole, *Bioorganic & Medicinal Chemistry Letters*, 16: 413-416.

[27]. Song, Ya-Li., Wu, Fan., (2015). Ionic liquid catalyzed of 2-(indole-3-yl)-thiochroman-4-ones and their novel antifungal activities, *Bioorganic & Medicinal Chemistry Letters*, 25: 259-261.

[28]. Husain, A., Ahmad, A., Abbasi, F.A., Khan, S.A., (2015). Synthesis and Anticonvulsant activity of indo-imidazolone Hybrid molecules, *Research & Reviews: Journal of Medicinal & organic Chemistry*, 1(1): 23-28.

[29]. Kumar, A., Kumar, D., (2011). Synthesis and evaluation of some newer indole derivatives as anticonvulsant agent, *International Journal Pharmaceutical & Biological Archives*, 2(2): 744-750.

[30]. Mirzaei, H., Shokrzadeh, M., Modanloo, M., Ziar, A., Riazi, G.H., Emami, S., (2017). New indole-based chalconoids as tubulin-targeting antiproliferative agents, Bioorganic Chemistry, 75: 86-89.

[31]. Choppara, P., Prasad, Y.V., Rao, C.V., Krishna, K.H., (2015). Design synthesis of novel *N* prenylated indole-3-carbazones and evaluation of *in vitro* cytotoxicity and 5-LOX inhibition activities, *Arabian Journal of Chemistry*, 3-8.