Recent Advancement of Indole Scaffolds with Pharmacological Potential: A Critical Review

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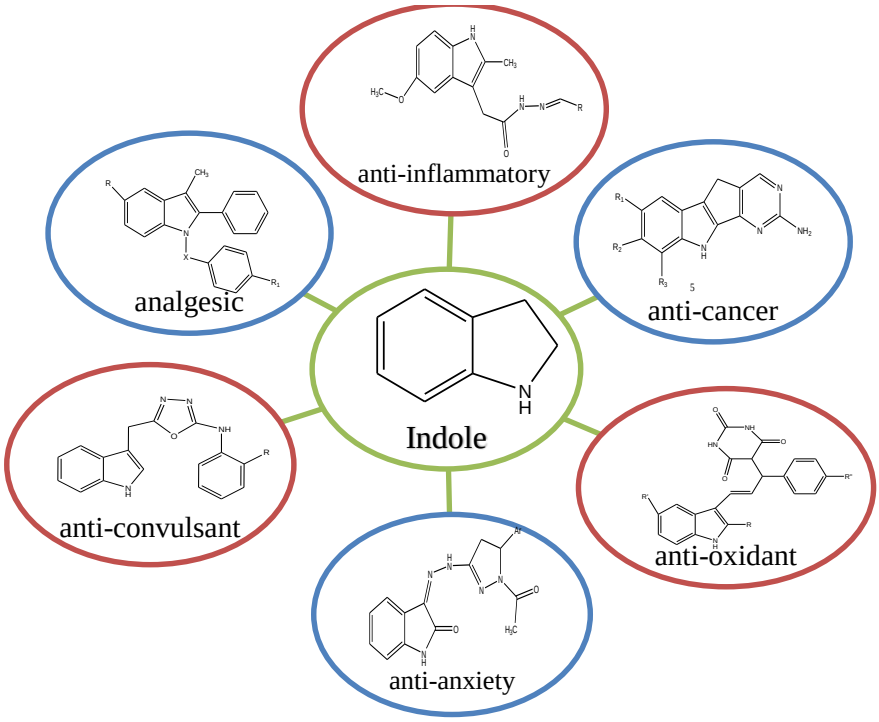
Abstract

Indole derivatives appear a significant class of heterocyclic compounds with diverse pharmacological and industrial applications. Characterized by a bicyclic structure comprising a benzene fused with pyrrole ring, these derivatives serve as core scaffolds in natural alkaloids, pharmaceuticals, and agrochemicals. Indole derivatives produced a wide range of pharmacological activities, including anticancer, antimicrobial, NSAIDs, and neuroprotective effects. Their synthetic modifications enable fine-tuning of physicochemical properties, enhancing drug-like characteristics. Advances in medicinal chemistry have led to novel indole-based therapeutics, with ongoing research focused on optimizing potency and selectivity. This review explores the structural diversity, biological significance, and recent advancements in the synthesis and applications of indole derivatives.

Keywords: Anti-inflammatory, Analgesic, Anti-convulsant, Anti-cancer activity, Anti-diabetic,

Graphical abstract



1. INTRODUCTION

Indole, often referred to as benzopyrrole, comprises a benzenoid structure and has a total of 10 π electrons **Fig. 1** (2 from the nitrogen's lone pair and 8 from the double bonds), rendering it aromatic. Like the benzene ring, indole readily undergoes electrophilic substitution because of the abundant delocalization of π-electrons.[1-3] The incorporation of the indole structure into medicinal compounds that possess biological activity has established it as a significant heterocyclic compound with a wide range of biological effects.[4] Numerous natural compounds have indole as their core structure, such as tryptophan. In more plants, indole-3-acetic acid, a plant hormone, is generated through the breakdown of tryptophan. Due to their varied biological and clinical uses, indole derivatives are of significant interest. In this summary, we aim to highlight the key pharmacological activities of indole derivatives.[5,] Indole derivatives produced a wide range of pharmacological activities, including. Antiviral[6,7] NSAIDs[8-10], anticarcinogenic[11-13], Antiretroviral therapy[14,15], antioxidant[16-18], antimicrobial[19,20], antitubercular[21], antidiabetic[22], antimalarial[23-25], anticholinesterase activities[26], etc. Numerous techniques have been outlined in the literature for the preparation of substituted indoles. Some of these techniques include the Fischer indole synthesis [27], the use of aryl bromides and allyl alcohols[28], the reaction of N-nitrosoanilines with alkynes[29], the reaction of o-bromonitrobenzenes with various vinyl Grignard reagents[30], and the interaction of o-nitrobenzyl cyanides with boronic acids[31]. Despite the availability of these methods, they have found numerous applications in creating novel indoles.

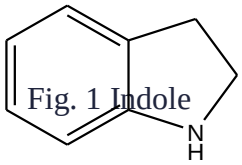
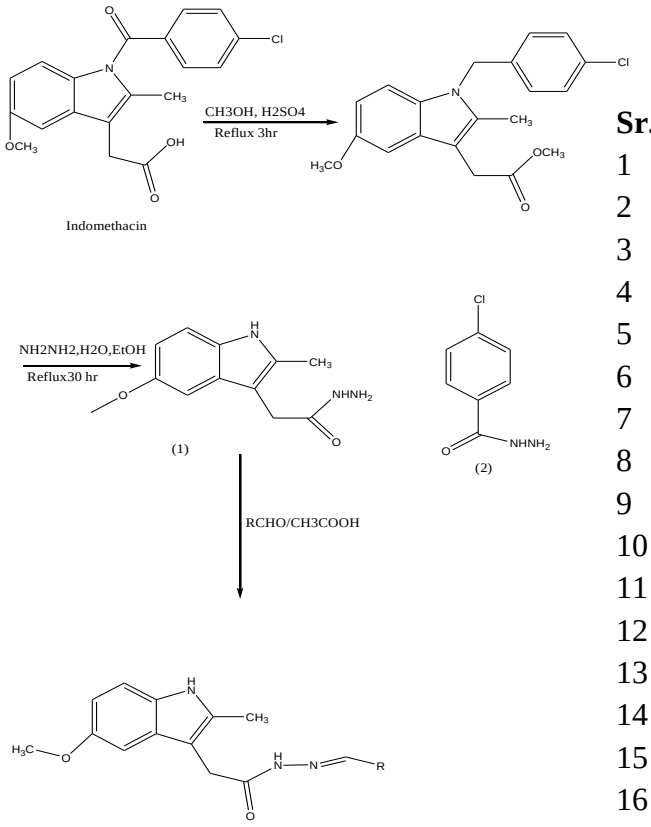


Fig. 1 Indole

- Anti-inflammatory
- Analgesic
- Anti-convulsant
- Anti-cancer
- Anti-oxidant
- Anti-anxiety

2. Material and methodology



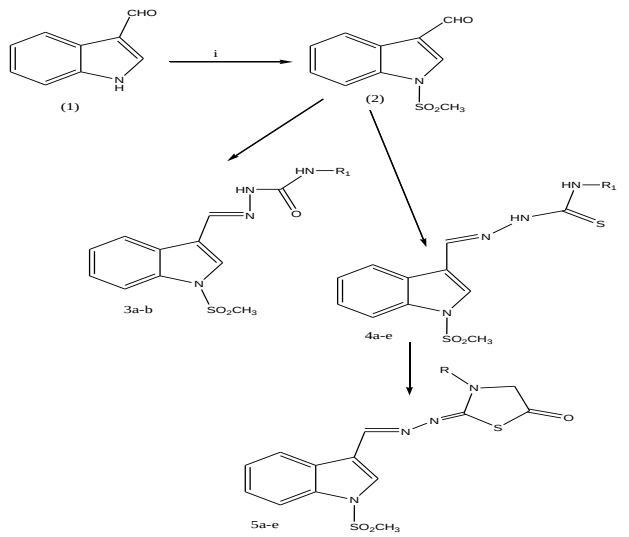
Sr.No.	Compound	R
1	A1	Phenyl
2	A2	4-nitrophenyl
3	A3	3-nitrophenyl
4	A4	2-nitrophenyl
5	A5	4-chlorophenyl
6	A6	2,4-dichlorophenyl
7	A7	3,4-dimethoxyphenyl
8	A8	2-methoxyphenyl
9	A9	4-hydroxyphenyl
10	A10	3- hydroxyphenyl
11	A11	4-dimethylaminophenyl
12	A12	3- methoxyphenyl
13	A13	4- ethoxyphenyl
14	A14	2,4,5-trimethoxyphenyl
15	A15	2,3,4- trimethoxyphenyl
16	A16	3,4,5- trimethoxyphenyl
17	A17	2,4,6- trimethoxyphenyl
18	A18	2,4- dimethoxyphenyl

Scheme 1. Synthetic Route of indole Compound (A1-A18)

Specifically, A3, 7, &14, demonstrated significant anti-inflammatory properties when compared to the reference medication indomethacin. These compounds were identified as powerful anti-inflammatory and analgesic agents in the following order: A14 > A3 > A7. Additionally, these compounds were found to cause fewer ulcers than the reference drug

indomethacin, with the order being A3 > A7 > A14. Compound A3, which contains a 3-nitrophenyl group, shows strong anti-inflammatory and analgesic effects while also having noteworthy stomach-sustaining activity. The formulation of lead compound A3 significantly minimizes stomach ulcers and reduces fat peroxidation.

The toxicity associated with A3 was found to be very low, and it exhibits considerable gastric activity. Notably, the substitution of 3-nitrophenyl hydrazides has a substantial impact on anti-inflammatory and analgesic actions while decreasing ulcerogenic activity. All these characteristics position A3 as a promising lead compound, warranting further biological investigations. Moreover, it was identified as an effective inhibitor of cyclooxygenase-2 expression. Studies indicated that this series of compounds (A1-18) could interact with cyclooxygenase-2 by formed a H bond involving the OH group of Tyr 355 and the amine group of Arg 120, along with the carbonyl group. This H bonding pattern resembles that of indomethacin. Identify critical insights for the advancement of novel anti-inflammatory and analgesic medications together gastroprotective properties.[32]

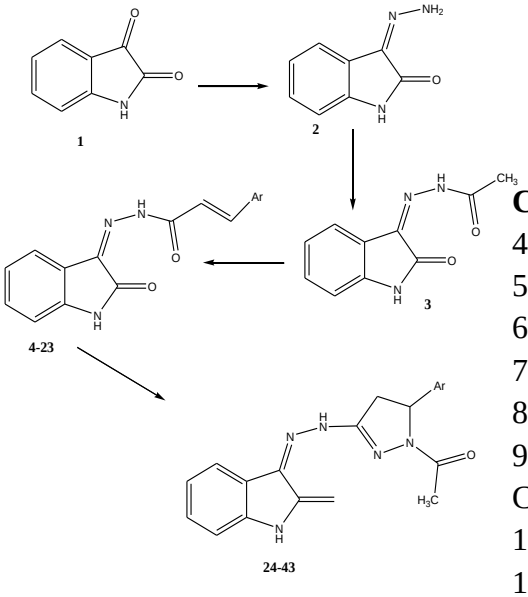


Compound	R	R1
3a	H	-
3b	C_6H_6	-
4a	-	H
4b	-	C_2H_5
4c	-	C_6H_6
4d	-	P-CH_3-C_6H_4,
4e	-	P-OCH_3-C_6H_4,
5a	-	H
5b	-	C_2H_5
5c	-	C_6H_6
5d	-	P-CH_3-C_6H_4,
5e	-	P-OCH_3-C_6H_4,

Scheme-2. Synthetic route of indole semicarbazide 3a&3b, thiosemicarbazide 4a-e, and thiazolidinone 5a-e derivatives

Three novels have been developed from derivatives of N-methylsulfonylindole 3a&b, 4a-e, and 5a-e. The examination of the biological activity of these synthetic compounds is currently ongoing. Antibacterial tests reveal that compounds 4b, 4d, and 5d exhibit selective antibacterial properties against diderm bacteria as well as E. coli. Antioxidant activity of synthetic derivatives was evaluated using 2,2-Diphenyl-1-picrylhydrazyl, Arc-en-Ciel method. Additionally, in vitro assessments of anti-inflammatory activity showed that compounds 4d, 4e, 5b, and 5d demonstrated the greatest anti-inflammatory effects. COX-1 and COX-2 inhibitory activities, along with 5-LOX, were measured using enzymatic immunoassay (EIA) kits. Due to the dual inhibitory effect of compound 5d on COX-2 and 5-Lipoxygenase, its

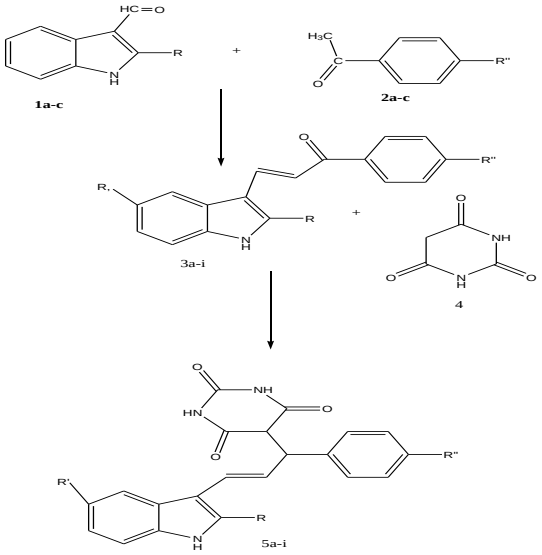
cardiovascular profile was assessed by evaluating cardiac biomarkers such as LDH, CK-MB, and Tn-I.[33]



Compound	-Ar	Compound	-Ar
4,24	C_6H_5-	14,34	4-CH_3-C_6H_4-
5,25	4-Cl-C_6H_4-	15,35	2-OCH_3-C_6H_4-
6,26	4-C_6H_5-CH_2O-C_6H_4-	16,36,	4-OCH_3-C_6H_4-
7,27	2-NO_2-C_6H_4-	17,37	2-Cl-C_6H_4-
8,28	4-OH-C_6H_4-	18,38	2-Br-C_6H_4-
9,29	4-OH,3-OCH_3-C_6H_3-	19,39	2,4-$(OCH_3)_2$-C_6H_3-
10,30	4-$(CH_3)_2$-N-C_6H_4-	20,40	4-NO_2-C_6H_4-
11,31	3-NO_2-C_6H_4-	21,41	2,3-$(OCH_3)_2$-

Scheme 3. Synthesis of the target indole derivatives.

A series of compounds identified as numbered 24 to 43, were synthesized through a suitable synthetic pathway and subjected to evaluation through the maximal electroshock test. These derivatives were assessed for their potential decrease depression and decrease anxiety effects. 25 Compound with the highest activity. comparison to the standard medication diazepam.[33]

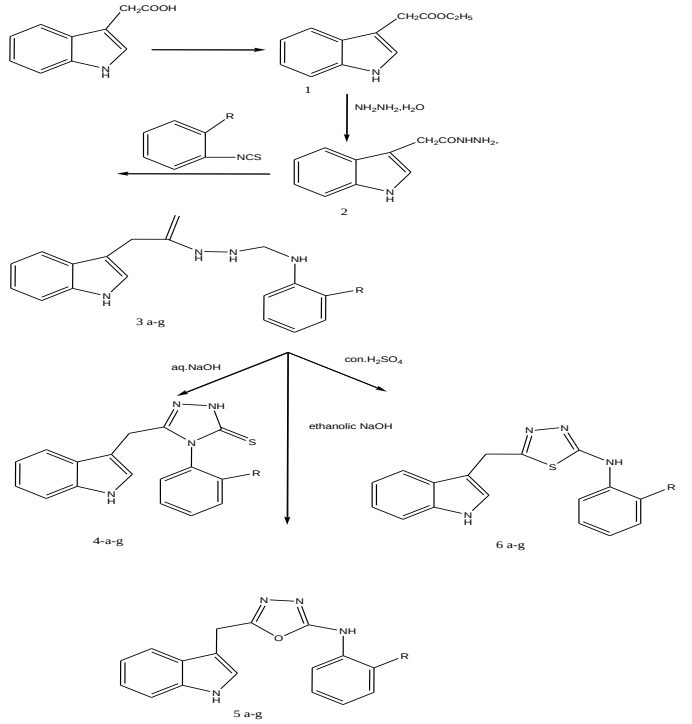


Compound	R	R’	R’’
5a	H	H	H
5b	Ph	CH_3	H
5c	Ph	Cl	H
5d	H	H	CH_3
5e	Ph	CH_3	CH_3
5f	Ph	Cl	CH_3
5g	H	H	Cl
5h	Ph	CH_3	Cl
5i	Ph	Cl	Cl

Scheme 4. Various synthesis route of indole derivatives

A novel series of indole derivatives incorporating a portion of Barbiton (5A-I) has been synthesized through a straightforward & suitable distillation of chalcon (3a-i) and barbituric acid (4). Resulting synthetic derivatives were assessed for their antioxidant properties (ability

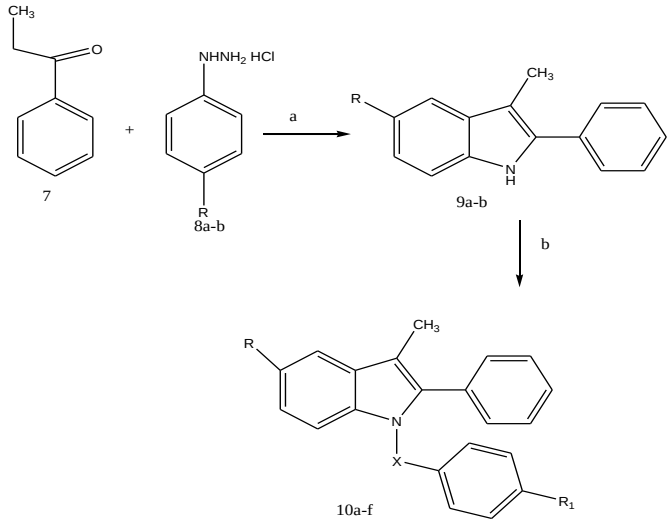
to absorb free radicals, overall antioxidant capacity, and iron reduction) as well as their impact on DNA mitotic activity. Out of the compounds, (5a), (5d), and (5g) demonstrated very good free-radical scavengers' performance, while all compounds in the series were subjected to testing.[34]



COMPOUND (3,4,5,6)	R
A	H
B	2-Cl
C	2-OCH_3
D	4--OCH_3
E	2-CH_3
F	3-CH_3
G	4-CH_3

Scheme 5. Various Indole derivatives

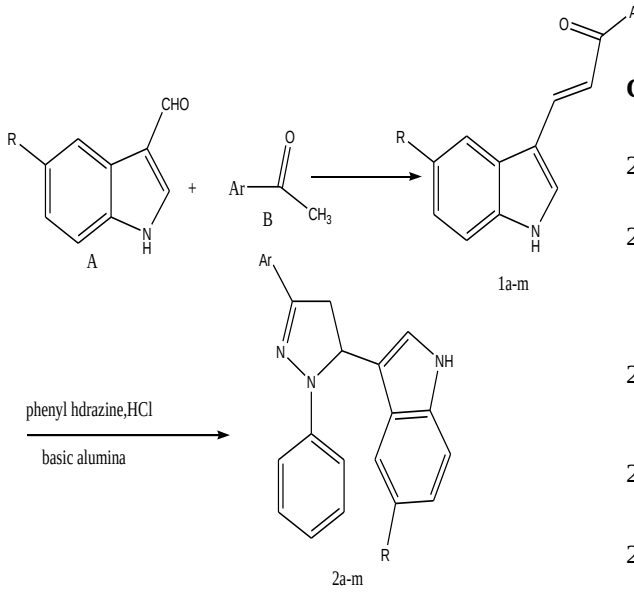
A novel series of indole 4a-g, 5a-g, & 6a-g react with 3a-g with acceptable chemicals. The synthesized derivatives were tested for anticonvulsant properties using the maximal electroshock seizure model, with results correlate with standard treatments. the 21 derivatives assessed, 4b, e, f, 5b, d, g, 6b, d, & 6e produced maximal electroshock seizure activity similar of phenytoin and carbamazepine after 30 minutes. Importantly, 5b demonstrated a higher potency than carbamazepine after four hours. Furthermore, derivatives 4a, c, d, 5a, c, e, f, 6f, & 6g exhibited reduced neurotoxicity in comparison to phenytoin.[35]

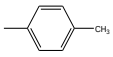
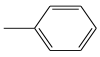
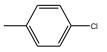
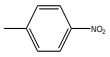
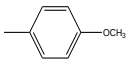
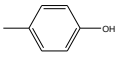
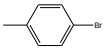
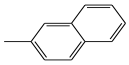


Compound	R	R^1	X
8a	H	-	-
8b	SO_2CH_3	-	-
9a	H	-	-
9b	SO_2CH_3	-	-
10a	H	H	CO
10b	h	Cl	CO
10C	H	H	CH_2
10d	SO_2CH_3	CO	H
10e	SO_2CH_3	CO	4-Cl
10f	SO_2CH_3	CH_2	H

Scheme 6. Various Indole derivatives

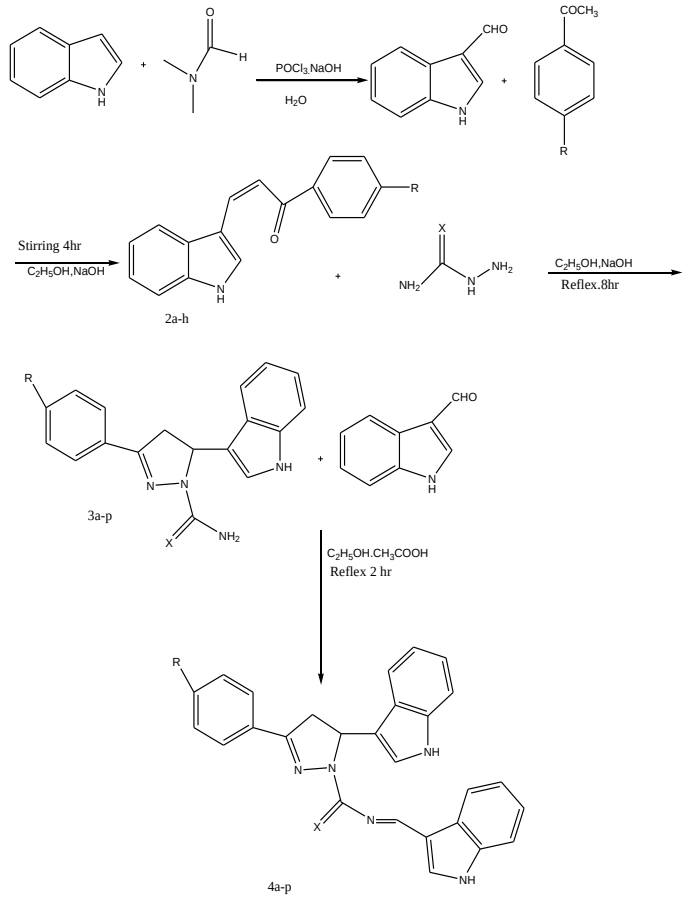
Six novel compounds, designated as 10a–f, were synthesized as derivatives of indomethacin for the purpose of biological evaluation regarding their NSAIDs. The in vitro studies assessing anti-inflammatory activity revealed synthesized derivatives exhibited greater accuracy for cyclooxygenase-2 compared to indomethacin, which had a COX-2 selectivity index of 0.055. Notably, compound 10e demonstrated an impressive 467-fold increase in COX-2 selectivity relative to indomethacin. Furthermore, in vivo studies on anti-inflammatory properties indicated that compounds 10d, 10e, & 10f, which incorporate SO2Me as a COX-2 pharmacophore, exhibited significant anti-inflammatory effects (ranging from 57.9% to 80.1%), comparable to those of indomethacin (71.2% to 88.4%), with compound 10d showing a range of 73.1% to 80.1% and compound 10e ranging from 71.8% to 73.5%.[36]



Compound	Ar	R	Compound	Ar	R
2a		H	2h		Br
2b		H	2i		
	OCH_3				
2c		H	2j		H
2d		H	2k		H
2e		H	2l		H
2f		H	2m		H
2g		H			

Scheme 7. Synthesis of pyrazole & indole derivatives.

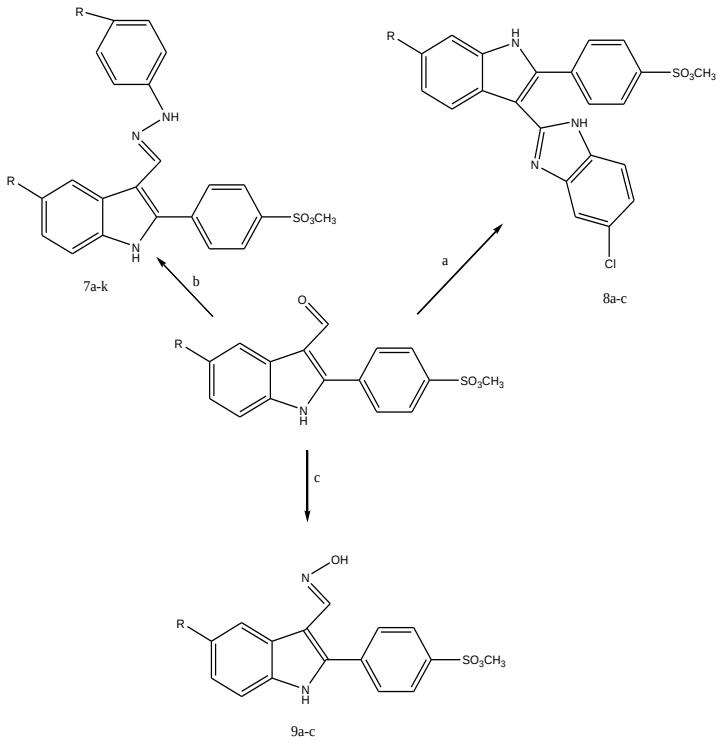
The substances (2e), (2b), & (2k) exhibited the most significant antidepressant effects, greatly reducing the duration of immobility dosage 100 mg/kg in comparison to the control group. Furthermore, the active derivatives 2b, 2e, and 2k also demonstrated considerable antidepressant effects at an IP dose of 20 mg/kg, when compared to imipramine and fluoxetine. When assessing compounds with various halogen substituents on the benzene ring, the properties was observed to follow the order of chlorine > Bromine > NO2, which decrease in the antidepressant effectiveness of the pyrazoline derivatives currently under investigation.[36]



Compound	X	R
4a	-O	-H
4b	-O	$-CH_3$
4c	-O	$-C_2H_5$
4d	-O	$-OCH_3$
4e	-O	$-NO_2$
4f	-O	-Cl
4g	-O	-OH
4h	-O	$-N(CH_3)_2$
4i	-S	-H
4j	-S	$-CH_3$
4k	-S	$-C_2H_5$
4l	-S	$-OCH_3$
4m	-S	$-NO_2$
4n	-S	-Cl
4o	-S	-OH
4p	-S	$-N(CH_3)_2$

Scheme 8. Synthesis various indole derivatives

The final products are R-substituted 4(a-p). The compounds synthesized were determined through infrared, mass, and nuclear magnetic resonance spectroscopy methods. The hypoglycaemic effect of these derivatives was assessed via both in vitro and in vivo methodologies. In the in vivo experiments, derivatives 4a and 4m exhibited moderate anti-effects comparable to the known medication glibenclamide. In the in vitro analysis, compounds 4a, 4e, and 4m demonstrated moderate anti-diabetic activity similar to the reference drug acarbose.[37]

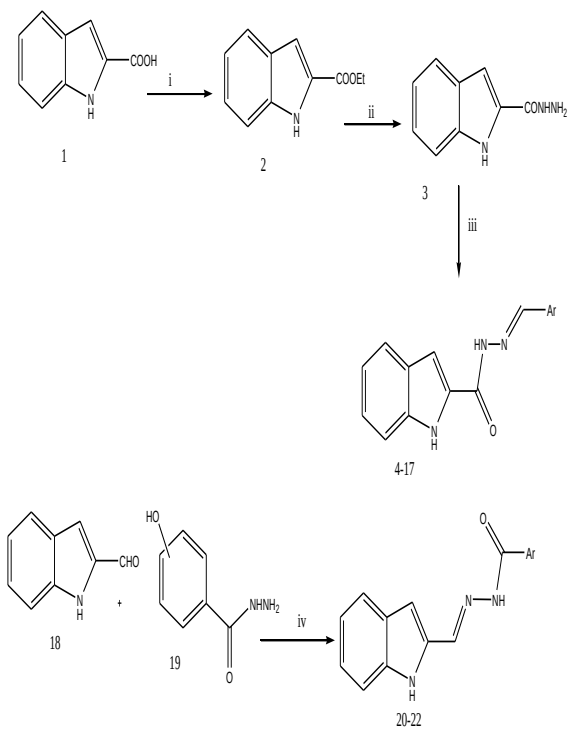


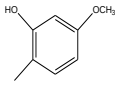
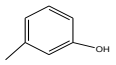
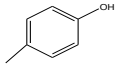
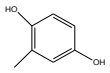
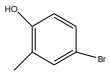
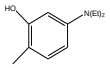
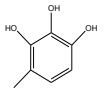
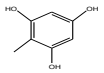
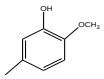
Compound	R	R_1
7a	H	F
7b	H	SO_2CH_3
7c	H	SO_2NH_2
7d	CH_3	SO_2CH_3
7e	CH_3	SO_2NH_2
7f	CH_3	F
7g	CH_3	CH_3
7h	F	SO_2CH_3
7i	F	SO_2NH_2
7j	F	F
7k	F	CH_3
8a	H	-
8b	F	-
8c	CH_3	-
9a	H	-
9b	F	-
9c	CH_3	-

Scheme 9. Various Indole derivatives

Three derivative series of indole was synthesized. Synthesized derivatives were tested for their antimicrobial, cyclooxygenase inhibition, properties. derivative 7g was found the most potent antibacterial agent against Methicillin-resistant Staphylococcus aureus, Escherichia coli, K. pneumoniae, P. aeruginosa, and A. baumannii, with a safe dosage. derivatives 7a–k, 8a–c, and 9a–c displayed noteworthy anti-inflammatory

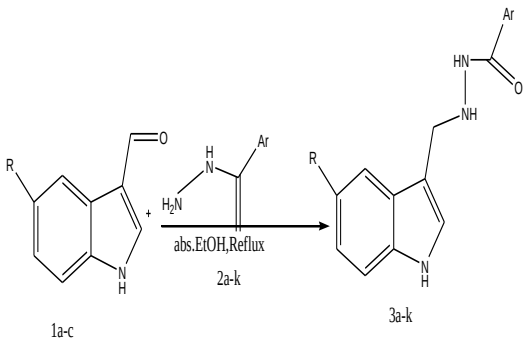
effects, showing a strong preference for COX-2 compared to the reference medications indomethacin and celecoxib. derivatives 9a–c was noted to release moderate amounts of NO, which could potentially mitigate the side effects typically associated with selective cyclooxygenase-2 inhibitors.[38]



Compound	Ar	Compound	Ar
4		12	
5		13	
6		14	
7		15	
8		16	
9		17	
10		20	
11		21	

Scheme 10. Various Indole derivatives

Two groups of indole compounds 4-17, 20-22 were easily synthesized and tested for their antioxidant properties. Compounds displayed different levels of antioxidant effectiveness in DPPH, FRAP, and ORAC assays. The presence and arrangement of -OH groups on the arylidene framework, along with the addition of methoxy or 4-(diethylamino) substitutions, correlated with enhanced antioxidant performance. compounds 4-17 demonstrated significant UV protection properties. Indoles 16 & 17, which showed the good antioxidant & photoprotective properties.[39]

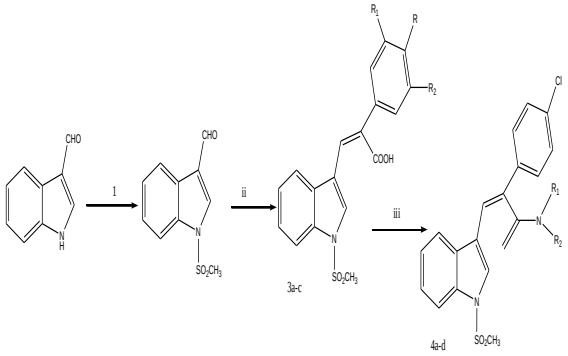


Compound	R	Ar
1a	OMe	-
1b	Br	-
1c	OCH_2Ph	-
2a	-	2-furyl
2b	-	3-pyridyl
2c	-	4-(N,N-dimethylamono)phenyl
2d	-	4-methoxypheny
2e	-	5-(4-methyl-1,2,3,thiadiazolyi)
2f	-	N-benzylpyrrolidinyl
2g	-	4-fluorophenyl
2h	-	3-pyridyl
2i	-	3-indolyi
		2j - 3-indolylaceto
2k	-	2-furyl
3a	OMe	2-furyl
3b	OMe	3-pyridyl
3c	OMe	4-(N,N-dimethylamono)phenyl
3d	OMe	4-methoxypheny
3e	OMe	5-(4-methyl-1,2,3,thiadiazolyi)
3f	OMe	N-benzylpyrrolidinyl
3g	Br	4-fluorophenyl
3h	Br	3-pyridyl
3i	Br	3-indolyi
3j	Br	3-indolylaceto
3k	OCH_2	2-furyl

Scheme 11. Various synthetic route for Indole

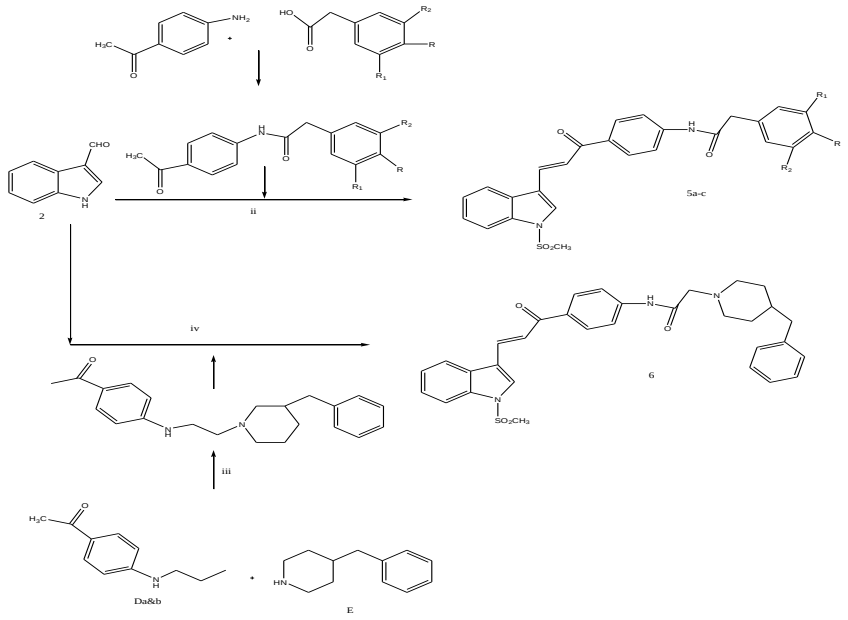
The compounds featuring a 5-methoxy substituted indole structure, specifically 3a, 3c, 3d, 3e, and 3f, along with those containing a 5-benzyloxindole structure like 3k, were identified as the most effective molecules, exhibiting MIC values between 0.39 and 0.77 µM. Consequently, compound 3e, which possesses a 4-methyl-1, 2,3-thiadiazolyl group and a 5-methoxyindole framework, proves to be an outstanding antimycobacterial agent, exhibiting double the potency compared to isoniazid and four times greater than ethambutol.

Additionally, the other synthesized derivatives with the indole structure and a methoxy substituent at the 5th position, namely 3c, 3d, 3f, and 3k, demonstrated significant antimycobacterial activity comparable to that of isoniazid.[40]



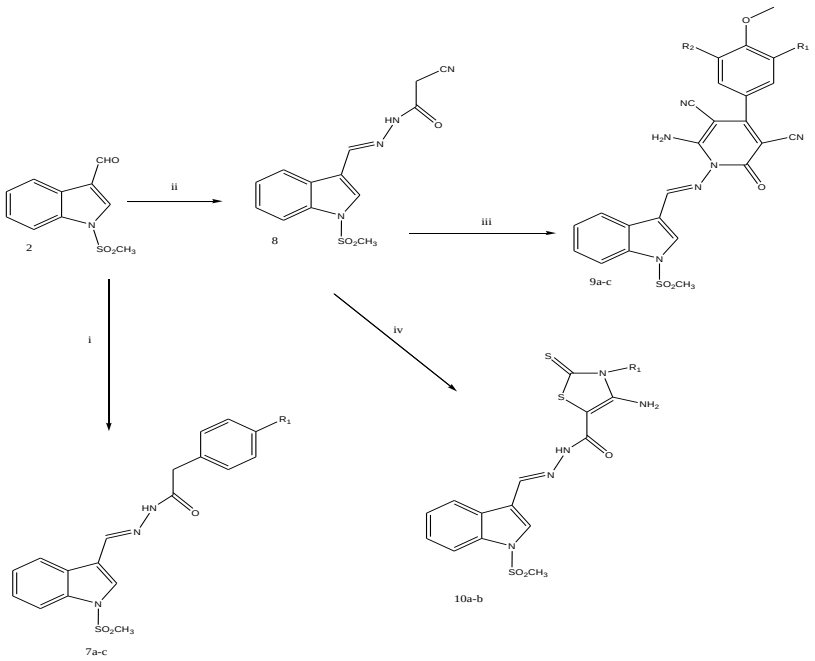
Compound	R	R1	R2
3a	H	H	H
3b	Cl	H	H
3c	OCH_3	OCH_3	OCH_3
4a	-	Pipridinyl	Pipridinyl
4b	-	3-aminopyridinyl	3-aminopyridinyl
4c	-	1-(2-pyrimidinyl)piprazineyl	1-(2-pyrimidinyl)piprazineyl
4d	-	1-benzylpipridinyl	1-benzylpipridinyl

Scheme 12. Synthetic route of indole derivatives



Compound	R	R1	R2
5a	H	H	H
5b	Cl	H	H
5c	OCH_3	OCH_3	OCH_3

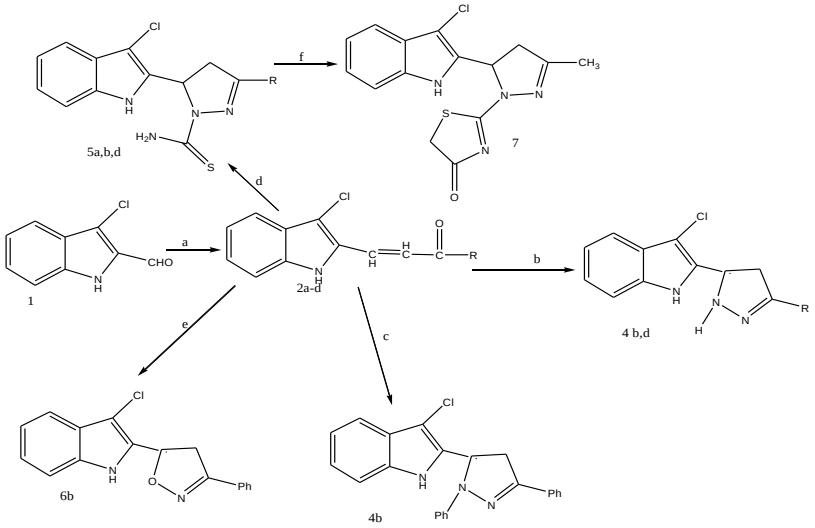
Scheme 13. Various synthetic route for preparation of chalcone derivative



Compound	R	R1
7a	H	-
7b	H	-
7c	Cl	-
9a	H	H
9b	OCH_3	H
9c	OCH_3	
	OCH_3	
10a	C_2H_5	-
10b	C_2H_5	-

Scheme 14. Synthetic routes for preparation of indole derivatives

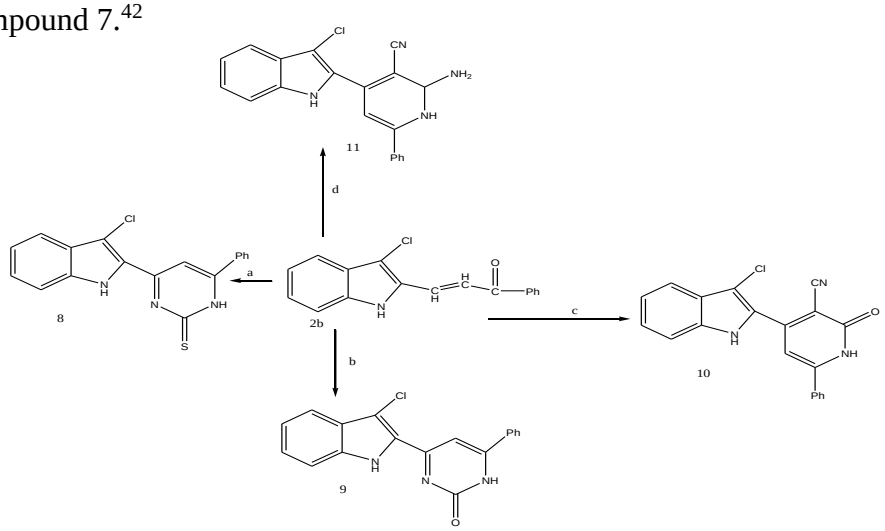
A new series of indole was synthesized, and test for their potential as agents against Alzheimer's & neuroinflammation. The synthesized derivatives underwent in vitro testing to assess their inhibitory effects on AChE and BuChE properties. The findings revealed that compound 3c showed more selectivity for AChE than for BuChE, while compounds 4a, b, & d exhibited a preference for BuChE over AChE. 5b, 6b, 7c, and 10b demonstrated double inhibitory activity against both AChE and BuChE. Additionally, compounds 5b & 6b were effective in inhibiting autogenic collection of Ab amyloid. derivatives 5b and 6b was analyse for a variety of anti-inflammatory mediators, including NO, COX-2, IL-1b, and TNF-a. Derivatives 5b & 6b used for the determination of cytotoxicity through In vitro test on human olfactory neuroblastoma and normal liver cell lines.[41]



Compound	R
a	CH_3
b	Ph
c	4-Cl-C_6H_4
d	4-CH_3O-C_6H_4

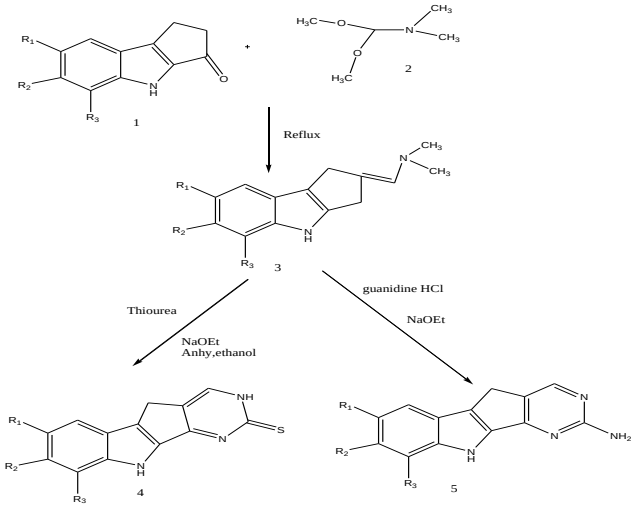
Scheme 15. Production of compounds of pyrazolyl and oxazolylindole

Derivatives 4b, 5b, 6b, and 7 shows anti-inflammatory activity when assessed against the standard treatment indomethacin. compounds 4b, 6b, and 7, with compound (4b) displaying more effectiveness in case of paw oedema inflammation because the active pyrazole ring is present. Two hours later activity of the tested compounds was notably more than one-hour mark, with derivative 4b & 5b exhibited equal activity (31.10%) out of all the derivatives tested, which was quite similar reference activity (33.33%); additionally, the effectiveness of compound 3b also showed an increase over time. After three hours, all the compounds examined showed further increases in activity, with derivative 4b and 5b, which include the pair of pyrazole ring together indole structure, continuing to demonstrate the highest activity along with compound 7.[42]



Scheme 16. Synthesis of pyridinyl and indole derivatives

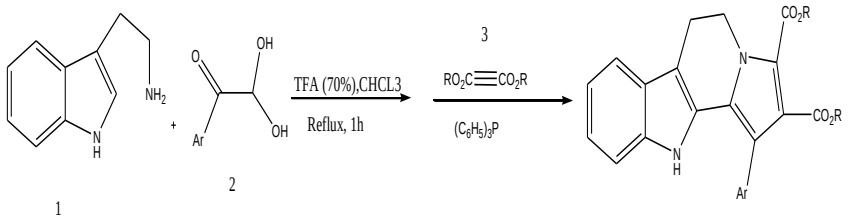
Out of all the examined fungal strains, derivative ten, which has a cyano group on the pyridine ring and an indole and pyridine core, had the strongest antifungal activity. Against Penicillium sp., compound 8 has antifungal properties comparable to those of normal ketoconazole, but compound 10 exhibits the least amount of activity against the same strain, indicating that this specific fungus reacts favorably to the pyrimidine structure present in compound 8. Compounds 8 and 10 had significant antifungal efficacy against S. racemosum, G. candidum, and Penicillium sp. Additionally, compounds 8 and 10 showed modest levels of activity against Candida albicans, whereas compound 9 showed the best antifungal efficacy.[43]



Compound	**R1**	**R2**	
	R3		
1,2,3,4,5a	H	H	H
b	CH_3	H	H
c	Cl	H	H
d	Br	H	H

Scheme 17. Synthesis of anticancer indole derivatives

Novel derivatives of indole were synthesized & test their anti-cancer properties. Derivatives 5c and 5d displaying significant anticancer effects. Through implementing a normal change in the structure, a novel potent anticancer agent designed with high activity. Furthermore, derivatives 5c and 4c showed excellent antibacterial activity compared to the standard treatments Sparfloxacin and Norfloxacin. [44]



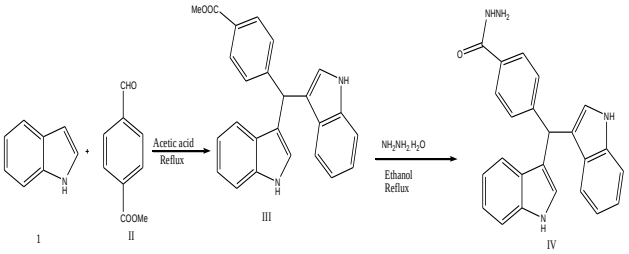
1 2

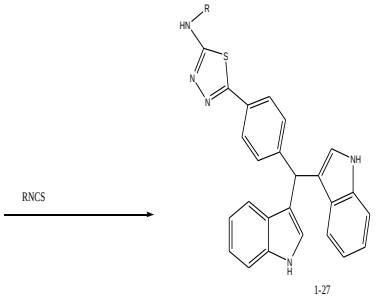
Compound	Ar	R	Compound	Ar	R
4a	Phenyl	CH_3	4j	Phenyl	CH_2CH_3
4b	4-methylphenyl	CH_3	4k	4-methylphenyl	CH_2CH_3
4c	3-methoxyphenyl	CH_3	4l	3-methoxyphenyl	CH_2CH_3
4d	4-methoxyphenyl	CH_3	4m	4-methoxyphenyl	CH_2CH_3
4e	4-chlorophenyl	CH_3	4n	4-chlorophenyl	CH_2CH_3
4f	3-bromophenyl	CH_3	4o	3-bromophenyl	CH_2CH_3
4g	4-bromophenyl	CH_3	4p	4-bromophenyl	CH_2CH_3
4h	4-nitrophenyl	CH_3	4q	4-nitrophenyl	CH_2CH_3
4i	Naphthalene-1-yl	CH_3	4r	Naphthalene-1-yl	CH_2CH_3

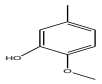
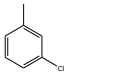
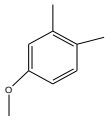
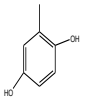
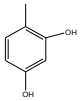
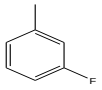
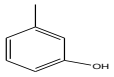
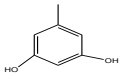
4a-r

Scheme 18. Indole derivatives 4a-r

A total of eighteen derivatives of indole, identified as 4a–r, was synthesized, and test for their potential as new (AGIs). These compounds generated using one-pot two-step method suitable conditions. The synthesized derivatives exhibited superior activity compared to the standard drug acarbose. derivatives 4o and 4h produced the most potent anti-α-glucosidase effects, with IC_{50} values of 107.2 ± 1.0 and 118.0 [45]



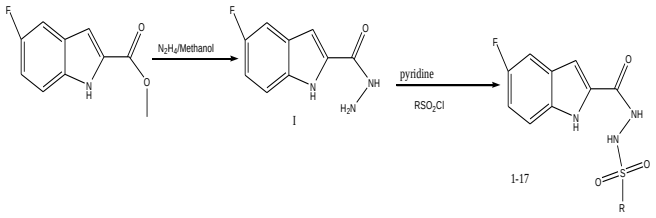


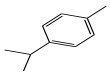
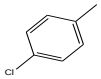
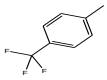
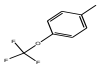
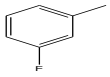
COMPOUND	R	COMPOUND	R
1		15	
2		16	
3		17	
4		18	
5		19	
6		20	
7		21	
8		22	
9		23	
10		24	
11		25	
12		26	
13		27	
14		-	

Scheme 19. Synthesis of bis-Indole Derivatives (1-27)

A novel group of anti-leishmanial agents was synthesized, consisting of a series of bisindole derivatives. We evaluated all compounds (1–27) for their efficacy against leishmania. Each

compound showed significant inhibition when compared to the standard treatment. In the 27 compounds, fifteen compounds—specifically 3, 4, 7, 8, 9, 11, 12, 15, 16, 17, 18, 20, 21, 22, & 25—demonstrated outstanding inhibitory effects. Derivatives 1, 2, 5, 6, 10, 13, 14, 19, 23, 24, 26, & 27 produced significant inhibitory properties, with IC_{50} values varying from 5.20±0.2 to 13.30±0.50 µM in relation along with standard. [46]



Compound	R	Compound	R
1		10	
2		11	
3		12	
4		13	
5		14	
6		15	
7		16	
8		17	
9		-	

Scheme 20. Synthesis of indole- based –sulphonamide derivatives 1-17

A novel series of indole derivatives was synthesized and tested their activities for inhibit the pancreatic α-amylase and intestinal α-glucosidase. The inhibition of carbohydrate-digesting enzymes is essential for creating new antidiabetic drugs. The compounds showed inhibitory property on α-amylase and on α-glucosidase, which are similar the acarbose. The derivatives numbered 4, 11, 12, 15, 14, and 17 exhibited significant promise in inhibiting both types of enzymes. [47]

3. Conclusion

Indole derivatives have proven to be invaluable scaffolds in medicinal chemistry, offering a wide range of biological activities that contribute to drug discovery and development. Their structural diversity and ease of modification have led to breakthroughs in anticancer, antimicrobial, anti-inflammatory, and neuroprotective therapeutics. Recent advances in synthetic methodologies, including green chemistry approaches and computational drug

design, have further enhanced their potential. In conclusion, indole derivatives remain at the forefront of pharmaceutical research, with ongoing efforts directed toward optimizing their properties for clinical applications. With continued advancements in synthetic techniques and a deeper understanding of structure-activity relationships, indole-based compounds are poised to contribute significantly to future drug discovery and therapeutic innovations.

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