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Research Article

INDOLE: THE MOLECULE OF DIVERSE BIOLOGICAL ACTIVITIES

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ABSTRACT

A large number of efforts were made to synthesize different heterocyclic compounds and their derivatives in the past decade and were found to posses promising antitumor, anticonvulsant, antimicrobial, anti-tubercular and anti diabetic activities. Although indole moiety is very small but is fascinated by scientists because of the diverse biological activities by not only indole but its various substituted derivatives as well. This review was focused on the indole and its derivatives that are now in development. Due to its wider applications in pharmaceutical industries, they will replace many existing heterocyclic based pharmaceuticals. Now days, many drugs are in the world market, while several hundred are in clinical trials.

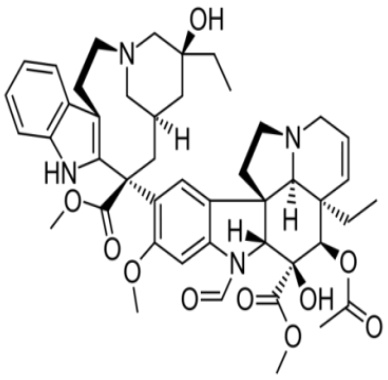
INTRODUCTION

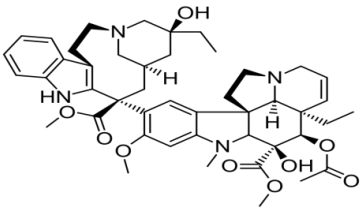
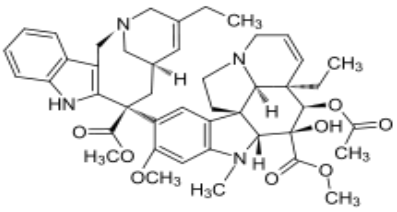
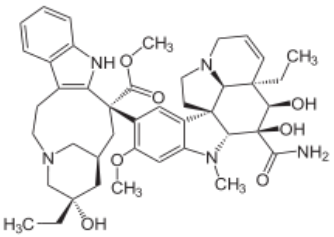
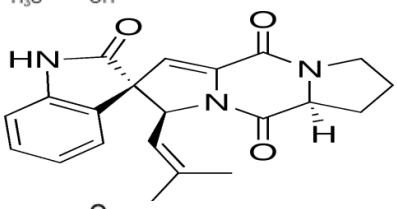
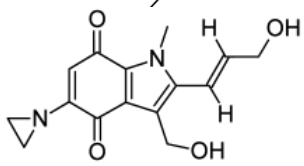
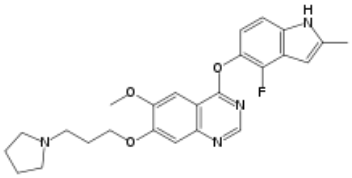
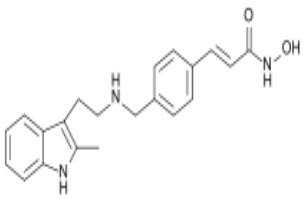
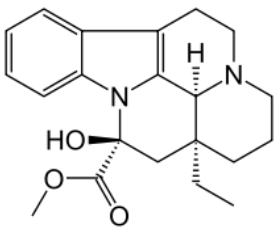
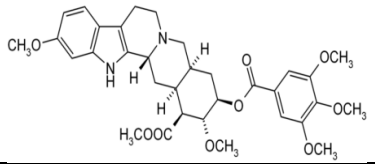
Medicinal chemistry is the discipline concerned with determining the influence of chemical structure on biological activity and in the practice of medicinal chemistry developed from an empirical one involving organic synthesis of new compound based largely on the modification of structure and then identifies their biological activity. Medicinal chemistry concerns with the discovery, development, interpretation and the identification of mechanism of action of biologically active compounds at the molecular level. Various biologically active synthetic compounds have five-member nitrogen-containing heterocyclic ring in their structures. An important aspect of medicinal chemistry has been to establish a relationship between chemical structure and pharmacological activity [1]. It has been established that half of the therapeutic agents consists of heterocyclic compounds. The heterocyclic ring comprises of very core of the active moiety or the pharmacophore[2]. **Indole** is an aromatic heterocyclic organic compound. It has a bicyclic structure, consisting of a six-membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. Indole is a popular component of fragrances and the precursor to many pharmaceuticals. Compounds that contain an indole ring are called indoles. Notably, the indolic amino acid tryptophan is the precursor of the neurotransmitter serotonin. In addition, indole ring is present in various marine or terrestrial natural compounds, which have useful biological properties. In last few years it was reported that indole, its bioisosters and derivatives had antimicrobial activity against Gramnegative, Gram-positive bacteria and the yeast *Candida albicans* and antimicrobial activity especially against *Enterobacter, Pseudomonas aeruginosa, E.coli,* and *Staphylococcus epidermidis*. Other activities involves are as follows.

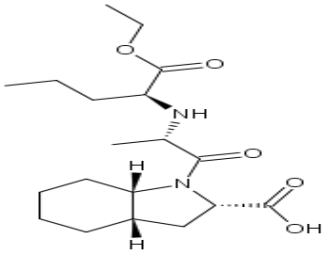
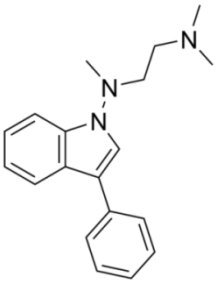
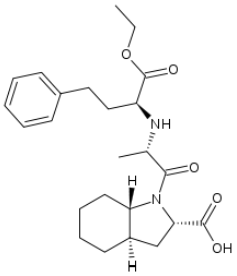
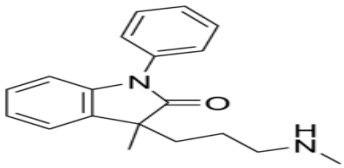
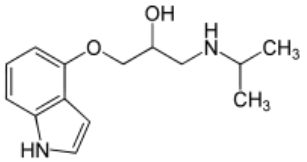
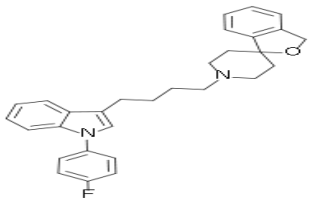
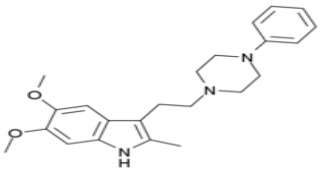
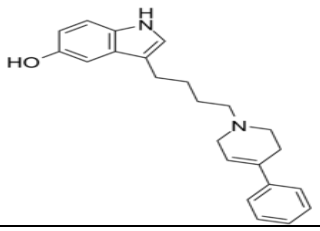
- Anti cancer drugs.
- Anti hypertensive drugs.
- Anti depressant drugs.
- Anti psychotic agents.
- NSAIDS.
- Anti emetic drug.
- Analgesic drug.
- Anti asthmatic drug.
- Anti viral drug.
- Anti arrhythmic drug.
- B-blocker drug
- Toxins.
- Inhibitor of RNA Polymerase-11.
- Agonist for the cannabinoid receptor.
- Non- Nucleoside reverse transcriptase inhibitor.
- Opioid agonist.
- Sexual dysfunction.

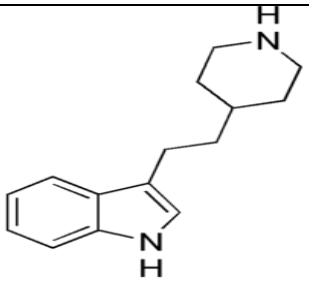
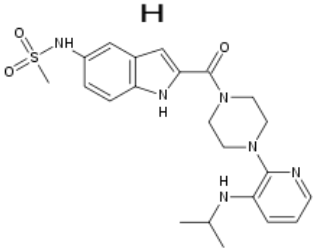
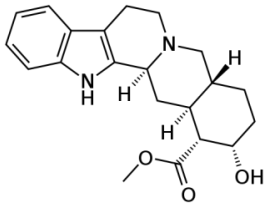
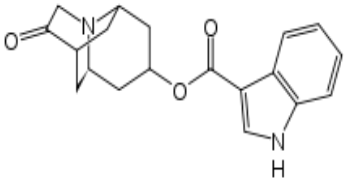
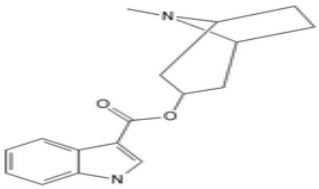
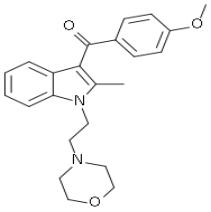
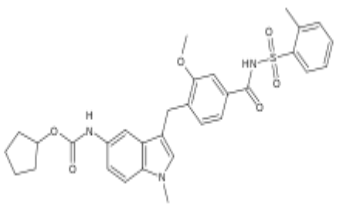
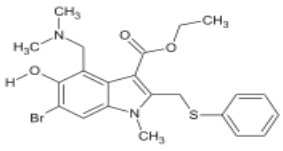
Given below is a brief account of various alterations conducted on indole ring containing few important marketed drug and their associated biological activities.

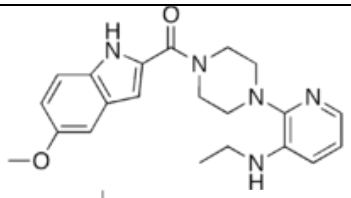
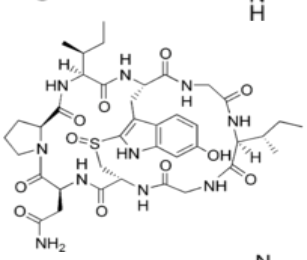
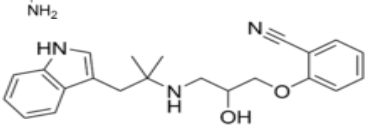
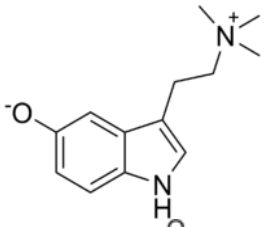
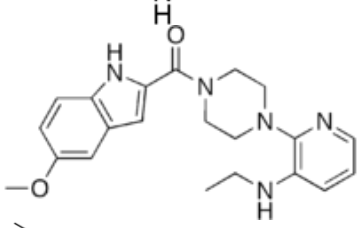
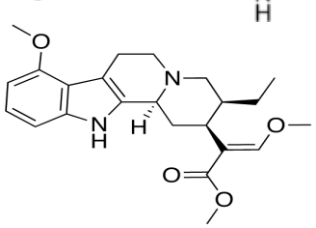
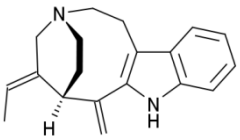
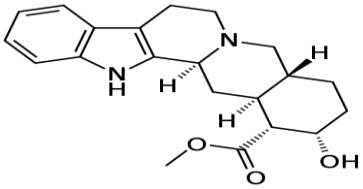
Table: Indole ring containing few marketed drug shows various biological activities

COMPOUND NAME	CHEMICAL STRUCTURE	USE	REFERENCES
VINCRISTINE (methyl (1*R*,9*R*,10*S*,11*R*,12*R*,19*R*)- 11-(acetyloxy)- 12-ethyl- 4-[(13*S*,15*S*,17*S*)- 17-ethyl- 17-hydroxy- 13-(methoxycarbonyl)- 1,11-iazatetracyclo[13.3.1.$0^{4,12}$.$0^{5,10}$]nonadeca- 4(12),5,7,9-tetraen- 13-yl]- 8-formyl- 10- hydroxy- 5-methoxy- 8,16-diazapentacyclo[10.6.1.$0^{1,9}$.$0^{2,7}$.$0^{16,19}$]nonadeca- 2,4,6,13-tetraene- 10-carboxylate .)		*ANTICANCER DRUGS*	**Jake Hooker et al.**[3]

VINBLASTINE (dimethyl (2β,3β,4β,5α,12β,19α)- 15-[(5*S*,9*S*)- 5-ethyl- 5-hydroxy- 9-(methoxycarbonyl)- 1,4,5,6,7,8,9,10-octahydro- 2*H*- 3,7-methanoazacycloundecino[5,4-*b*]indol- 9-yl]- 3-hydroxy- 16-methoxy- 1-methyl- 6,7-didehydroaspidospermidine3,4-dicarboxylate .)		*ANTICANCER DRUGS*	**Jordan MA et.al.[4]**
VINORELBINE (4-(acetyloxy)- 6,7-didehydro- 15-((2R,6R,8S)-4-ethyl-1,3,6,7,8,9-hexahydro- 8-(methoxycarbonyl)- 2,6-methano- 2H-azecino(4,3-b)indol-8-yl)- 3-hydroxy- 16-methoxy- 1-methyl- methyl ester, (2beta,3beta,4beta,5alpha,12R,19alpha)-aspidospermidine- 3-carboxylic acid)		*ANTICANCER DRUGS*	
VINDESINE (methyl (5S,7S,9S)- 9-[(2β,3β,4β,5α,12β,19α)- 3-(aminocarbonyl)- 3,4-dihydroxy- 16-methoxy- 1-methyl-6,7-didehydroaspidospermidin- 15-yl]- 5-ethyl- 5-hydroxy- 1,4,5,6,7,8,9,10-octahydro- 2H- 3,7-methanoazacycloundecino[5,4-b]indole- 9-carboxylate.)		*ANTICANCER DRUGS*	**Jordan MA, et.al[5]**
MITRAPHYLLINE (Mitraphylline)		*ANTICANCER DRUGS*	***García Giménez D* et.al.[6]**
APAZIQUONE **(**5-(1-Azirinyl)-3-(hydroxymethyl)-2-(3-hydroxy-1-propenyl)-1-methyl-1H-indole-4,7-dione **)**		ANTI MICROBIAL DRUGS	***Puri, R. et al.[7]***
CEDIRANIB **(**4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline**)**		potent inhibitor of VEGF receptor tyrosine kinases	***Wedge SR et al.[8]***
PANOBINOSTAT (N-hydroxy-3-[4-({[2-(2-methyl-1H-indol-3-yl)ethyl]amino}methyl)phenyl]acrylamide)		CUTANEOUS TCELL LYMPHOMA	***Prince, HM et al.[9]***
VINCAMINE (methyl(15R,17S,19R)-15-ethyl-17-hydroxy-1,11-diazapentacyclo[9.6.2.02,7.08,18.015,19]nonadeca-2(7),3,5,8(18)-tetraene-17-carboxylate.)		ANTI-HYPERTENSIVE DRUGS	**Cook, P.*et.al*[10]**
RESERPINE (methyl-11,17α-dimethoxy-18β-[(3,4,5-trimethoxybenzoyl)oxy]-3β,20α-yohimban-16β-carboxylate)		ANTI-HYPERTENSIVE DRUGS	**Chobanian AV et.al [11]**

PERINDOPRIL (2S,3aS,7aS)-1-[(2S)-2-{[(2S)-1-ethoxy-1-oxopentan-2-yl]amino}propanoyl]-octahydro-1H-indole-2-carboxylic acid		ACE INHIBITOR AND ANTIHYPERTENSIVE.	**Bounhoure JP et.al** [12]
BINEDALINE N,N,N-trimethyl-N-(3-phenylindol-1-yl)ethane-1,2-diamine		ANTI DEPRESSANT DRUGS	**Geerling, F.et.al** [13]
TRANDOLAPRIL (2S,3aR,7aS)-1-[(2S)-2-{[(2S)-1-ethoxy-1-oxo-4-phenylbutan-2-yl]amino}propanoyl]-octahydro-1H-indole-2-carboxylic acid.		ACE INHIBITOR ANTI DEPRESSANT DRUGS	**Geerling, F et.al** [14]
AMEDALIN (3-methyl-3-[3-(methylamino)propyl]-1-phenyl-1,3-dihydro-2H-indol-2-one)		ANTI DEPRESSANT DRUGS	**Canas-Rodriquez A et.al** [15]
PINDOLOL (1-(1H-indol-4-yloxy)-3-(isopropylamino)propan-2-ol)		ANTI DEPRESSANT DRUGS	**Isaac MT et.al** [16]
SIRAMESINE (1'-{4-[1-(4-fluorophenyl)-1H-indol-3-yl]butyl}-3H-spiro[2-benzofuran-1,4'-piperidine])		ANXIOLYTIC AND ANTIDEPRESSANT	**Romero AG et.al** [17]
OXYPERTINE (5,6-dimethoxy-2-methyl-3-[2-(4-phenylpiperazin-1-yl)ethyl]-1H-indole)		ANTI PSYCHOTIC AGENTS	**Hall, Chapman et.al**[18]
ROXINDOLE **3-[4-(4-phenyl-3,6-dihydro-2H-pyridin-1-yl)butyl]-1H-indol-5-ol**		SCHIZOPHRENIA	**F.A. Davis Company.**[19]

INDALPINE **(3-(2-piperidin-4-ylethyl)-1H-indole**		SEROTONERGIC ANTIDEPRESSANT DRUG	**Shopsin, B et.al[20]**
DELAVIRDINE N-[2-({4-[3-(propan-2-ylamino)pyridin-2-yl]piperazin-1-yl}carbonyl)-1H-indol-5-yl]methanesulfonamide		NON- NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR	**DHHS et.al [21]**
YOHIMBINE 17α-hydroxy-yohimban-16α-carboxylic acid methyl ester		SEXUAL DYSFUNCTION	**Ostojic SM et.al [22]**
DOLASETRON (10-oxo-8-azatricyclo[5.3.1.03,8]undec-5-yl 1H-indole-3-carboxylate)		ANTI EMETIC	**Katzung et.al [23]**
TROPISETRON **(8-methyl-8-azabicyclo[3.2.1]octan-3-yl 1methyl-indole-3-carboxylate)**		ANTI EMETIC	**Macor JE et.al [24]**
PRAVADOLINE ((4-methoxyphenyl)-[2-methyl-1-(2-morpholin-4-ylethyl)indol-3-yl]methanone)		ANALGESIC	**Bell MR et.al.[25]**
ZAFAIRLUKAST (cyclopentyl {3-[2-methoxy-4-({[(2-methylphenyl) sulfonyl]amino}carbonyl)benzyl]-1-methyl-1H-indol-5-yl}carbamate)		ANTI—ASTHMATIC	**Fischer JD et.al [26]**
ARBIDOL (1-methyl-2-((phenylthio)methyl)-3-carbethoxy-4-((dimethylamino)methyl)-5-hydroxy-6-bromindole)		ANTI VIRAL DRUG	**Leneva IA et.al[27]**

ATEVIRIDINE [4-[3-(ethylamino)pyridin-2-yl]piperazin-1-yl]-(5-methoxy-1H-indol-2-yl)methanone		NON- NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR	**Morse GD et.al** [28]
PROAMANULLIN 2-L-Proline-3-isoleucine-alpha-amanitin		INHIBITOR OF RNA POLYMERASE-11	**Cochet-Meilhac M et.al** [29]
BUCINDOLOL (2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethyl-ethyl]amino]propoxy]benzonitrile)		β-BLOCKER	**Willette RN et.al.**[30]
BUFOTENIDINE 3-[2-(Trimethylazaniumyl)ethyl]-1H-indol-5-olate		TOXINS	**Wieland et.al**[31]
ATEVIRIDINE (4-[3-(ethylamino)pyridin-2-yl]piperazin-1-yl]-(5-methoxy-1H-indol-2-yl)methanone)		ANTI-HIV	**Morse GD et.al.**[32]
MITRAGYNINE (2-[(2S,3S)-3-ethyl-8-methoxy-1,2,3,4,6,7,12,12b-octahydroindolo[3,2-h]quinolizin-2-yl]-3- methoxyprop-2-enoic acid methyl ester)		OPIOID AGONIST	**Takayama H et.al.**[33]
PERICINE (5-ethylidcene-1,4,5,6,7,8-hexahydro-7-methylene-2H-3,6-ethanoazonino(5,4-b)indole)		OPIOID AGONIST	**Margaret F.et.al** [34]
YOHIMBINE (1**7α**-hydroxy-yohimban-16α-carboxylic acid methyl ester)		SEXUAL DYSFUNCTION	**Rosengren, A. H. et.al** [35]

CONCLUSION

The reviewed indole moiety has shown a wide spectrum of biological activities. The various substituted indole and are having significant antibacterial activity. Significant analgesic, anti-inflammatory, antipyretic and anti tumor activity is displayed by some effective substituted indole derivative which presently leading drug in the market in entire. some modified indole are found to to be effective as anti-hypertensive , anti depressant, opoid antagonist & anti emetic agent agents, whereas some of the derivatives of indole are found to show the anti-asthmatic, anti;viral as special anti HIV action. Recently it was proven that the yohimbine act as a potent drug in sexual dysfunction. some of the important marketed indole nucleus containing drug having different biological or pharmacological activity were discussed in table. The indole nucleus based pharmaceutical are rapidly becoming very important class of therapeutic agents and are likely to replace many existing organic based pharmaceuticals in the very near future. The indole based pharmaceuticals will be produced on a large scale by modern drug discovery company by different research development processes and will become available commercially for therapeutic use. With the key benefits including favorable time to market and high rate of success in clinical trial compared with traditional pharmaceuticals due to diverse biological action with less toxicity, so in future therapeutic indole drug will play a pivotal role in the treatment of

different diseases. The biological profiles of this new generation of indole represent much progress with regard to the older compounds.

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