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Review Article

Review of indole, A versatile pharmacophoric moiety

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ABSTRACT

Indole is a heterocyclic compound, known for its alluring smell. Indole contributes to the rich aroma of various flowers such as jasmine and orange blossoms. Indole plays a vital role in numerous biological processes, including hormone regulation, neurotransmission, and immune response. Indole derivatives serve as a foundation for developing drugs in several therapeutic areas, such as antiviral, anticancer, and psychiatric medications.

1. Introduction

Indole is a heterocyclic aromatic compound composed of a bicyclic structure. It consists of a six-membered benzene ring fused to a five-membered pyrrole ring, resulting in a unique and intriguing chemical structure. Found in various natural products such as serotonin, tryptophan, and auxins.

1. ***Reactivity*** *:* Reacts with electrophiles, nucleophiles, radicals, and metals to afford a wide range of substituted indole derivatives.
2. ***Functional Groups****:* Indole derivatives can have a wide range of functional groups, including halogens, amines, ketones, esters, and more.

Indole Exhibits antimicrobial, anticancer, anti-inflammatory, and neuromodulator activities.

2. Review

2.1. Drugs containing Indole Ring have been reviewed in this section.

Drugs Containing indole ring/derivatives:

Properties	
Chemical Formula	C8H7N
Molecular Mass	117.124 g/mol
Appearance	White Solid turn yellow on exposure to light.
Melting Point	52-54 degrees Celsius
Acidity(pKa)	16.2
Basicity(pKb)	17.6

1. Anticancer
2. NSAID
3. Antiemetic
4. ED (Erectile Dysfunction Drugs)
5. Antimigraine agents
6. Antiviral

3. Anticancer Drugs

There are several U.S FDA has recently approved indole based anticancer agents such as

1. Vinblastine
2. Panobinostat
3. Alectinib

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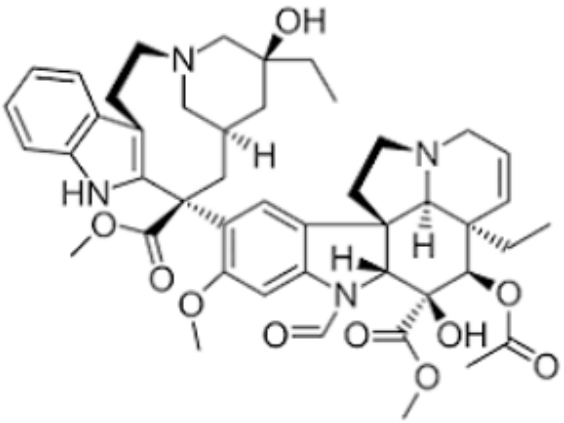
4. Sunitinib
5. Osimertinib
6. Nintedanib

4. Vinblastine



Vinblastine sulfate[1,2] has the molecular formula C46H58O9N4• H2SO4 and it is a dimeric alkaloid containing both indole and dihydroindole moieties.

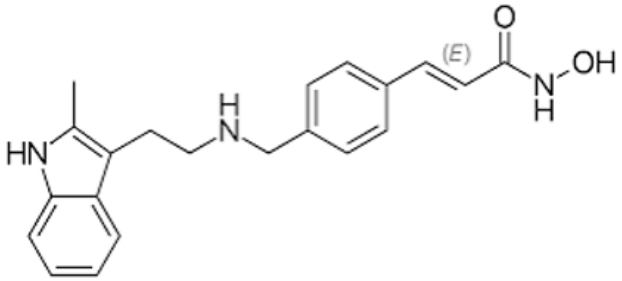
IUPAC: Dimethyl(2β,3β,4β,5α,12β,19α)-15-[(5S,9S)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2H-3,7-methanoazacycloundecino[5,4-b]indol-9-yl]-3-hydroxy-16-methoxy-1-methyl-6,7-didehydroaspidospermidine-3,4-dicarboxylate.

MOA: It binds to microtubular proteins in the mitotic spindle, thereby preventing cell division during metaphase. It also interferes with amino acid metabolism by inhibiting glutamic acid utilization and preventing purine synthesis, citric acid cycle, and urea formation.

5. Marketed Preparation

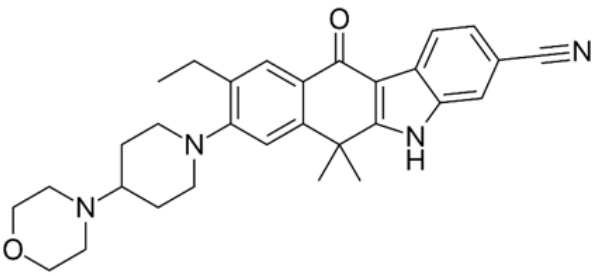
5.1. Other anticancer drugs

5.2. Panobinostat



Panobinostat[3,4] sold under the brand name Farydak, is a medication used for the treatment of multiple myeloma. It is a hydroxamic acid and acts as a non-selective histone deacetylase inhibitor (pan-HDAC inhibitor). Panobinostat is used in combination with the anti-cancer drug bortezomib and the corticoid dexamethasone for the treatment of multiple myeloma in adults who had received at least two previous treatments, including bortezomib and an immunomodulatory agent.

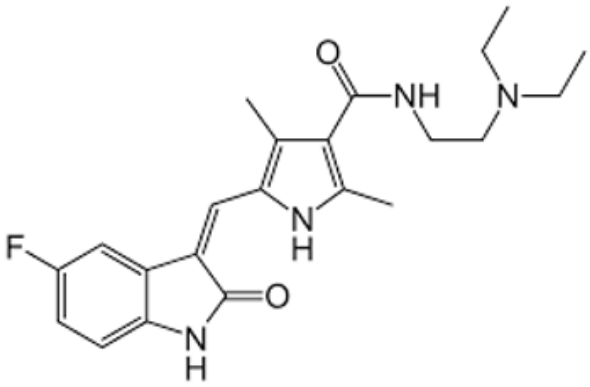
5.3. Alectinib



IUPAC: 9-Ethyl-6,6-dimethyl-8-[4-(morpholin-4-yl)piperidin-1-yl]-11-oxo-6,11-dihydro-5H-benzo[b]carbazole-3-carbonitrile

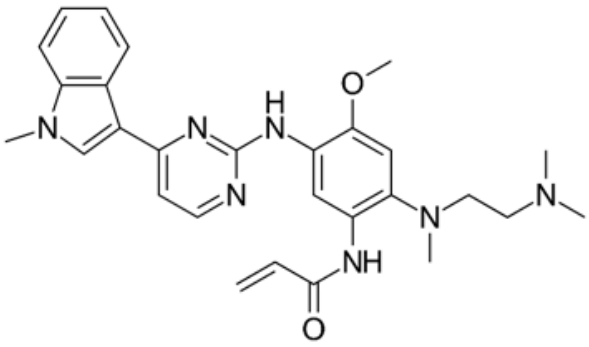
Alectinib[5,6] is indicated for the first-line treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC);[5] and for the treatment of adults with ALK‑positive advanced NSCLC previously treated with crizotinib.

5.4. Sunitinib



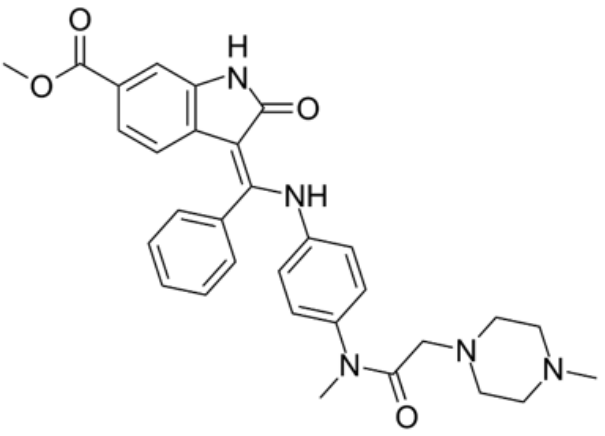
Sunitinib[7,8] sold under the brand name Sutent, is an anti-cancer medication. It is a small-molecule, multi-targeted receptor tyrosine kinase (RTK) inhibitor that was approved by the FDA for the treatment of renal cell carcinoma (RCC) and imatinib-resistant gastrointestinal stromal tumor (GIST) in January 2006. Sunitinib was the first cancer drug simultaneously approved for two different indications.

5.5. Osimertinib



Osimertinib[9,10] is used to treat locally advanced or metastatic non-small-cell lung cancer (NSCLC), if the cancer cells are positive for the T790M mutation in the gene coding for EGFR or for activating EGFR mutations. The T790M mutation may be de novo or acquired following first-line treatment with other EGFR tyrosine kinase inhibitors, such as gefitinib, erlotinib, and afatinib.

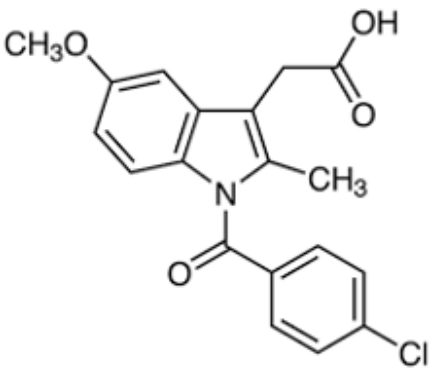
5.6. Nintedanib



Nintedanib[11,12] It is used in idiopathic pulmonary fibrosis and Lung Cancer.

6. NSAID

6.1. Indomethacin



IUPAC:2-{1-[(4-Chlorophenyl) carbonyl]-5-methoxy-2-methyl-1H-indol-3-yl}acetic acid

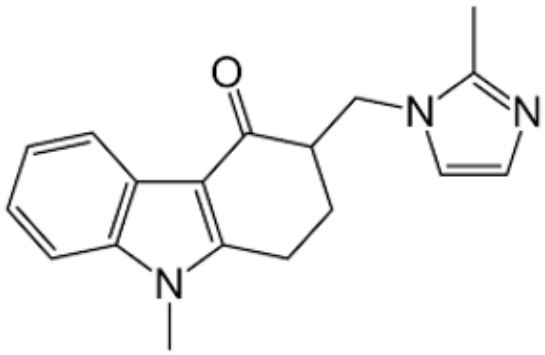
Indomethacin[13,14] is a nonsteroidal anti-inflammatory drug (NSAID) used to treat mild to moderate acute pain and relieve symptoms of arthritis (osteoarthritis and rheumatoid arthritis) or gout, such as inflammation, swelling, stiffness, and joint pain.

MOA: Inhibits the synthesis of prostaglandins and prostaglandin synthesis.

7. Marketed Preparation

8. Antiemetic

8.1. Ondansetron



IUPAC: (RS)-9-Methyl-3-[(2-methyl-1H-imidazol-1-yl)methyl]-2,3-dihydro-1H-carbazol-4(9H)-one

Ondansetron [15,16] is a selective antagonist of the 5-hydroxytryptamine3 (5-HT3) receptors and is a very effective agent in the prevention and treatment of nausea and vomiting. Ondansetron is used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy, and surgery. It works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting

8.2. Marketed preparations

9. ED (Erectile Dysfunction Drugs)

9.1. Tadalafil

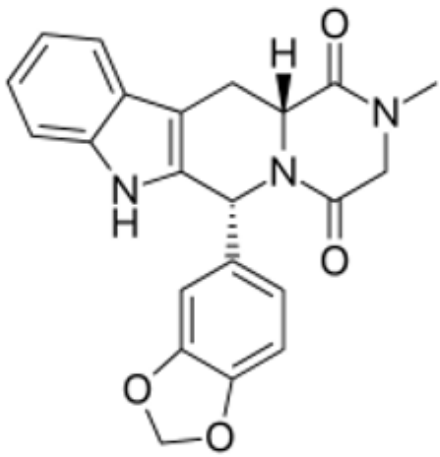


Figure 1:

IUPAC: (6R,12aR)-6-(1,3-benzodioxol-5-yl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino [1',2':1,6] pyrido[3,4-b]indole-1,4-dione

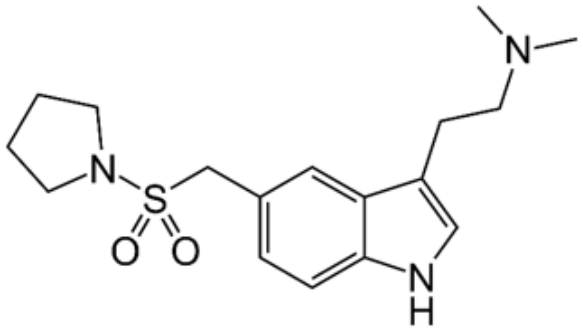
MOA : Tadalafil [17,18] is in a class of medications called phosphodiesterase (PDE) inhibitors. It works to treat erectile dysfunction by increasing blood flow to the penis during sexual stimulation.

10. Marketed Preparation

11. Antimigraine agents

MOA: Triptans group drugs act as antimigraine agents by selectively binding to the serotonin receptors 5-HT1B and 5-HT1D

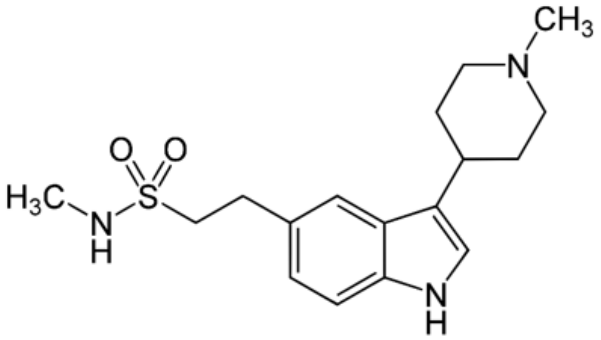
11.1. Almotriptan[19]



IUPAC: N, N-dimethyl-2-[5-(pyrrolidin-1-ylsulfonylmethyl)-1H-indol-3-yl] ethanamine

12. Marketed Preparation

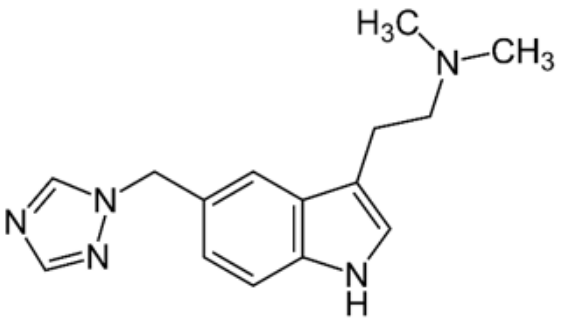
12.1. Naratriptan[20]



IUPAC: N-methyl-2-[3-(1-methylpiperidin-4-yl)-1H-indol-5-yl] ethane-1-sulfonamide hydrochloride.

13. Marketed Preparation

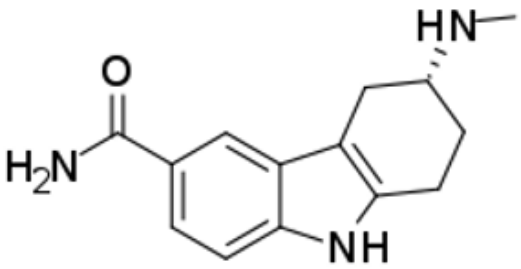
13.1. Rizatriptan[21]



IUPAC: - N, N-Dimethyl-2-[5-(1H-1,2,4-triazol-1-ylmethl)- y1H-indol-3-yl]ethanamine

14. Marketed Preparation

14.1. Frovatriptan[22]

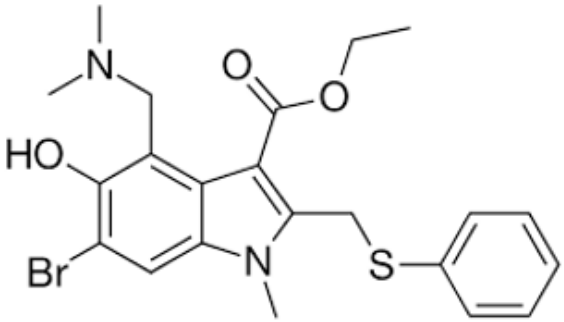


IUPAC: (+) -(R)-3-Methylamino-6-carboxamido-1,2,3,4-tetrahydrocarbazole

15. Marketed Preparation

16. Antiviral

16.1. Arbidol[23]



IUPAC: (2S,3R,4R,5R)-Hexane-1,2,3,4,5,6-hexol

17. Conclusion

Witness the broad spectrum of therapeutic applications of indole. From treating psychiatric disorders to combating microbial infections, indole-based drugs offer promising avenues for current and future medical treatments.

18. Source of Funding

None.

19. Conflict of Interest

None.

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Author biography

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