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Research Article

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A Review Article on Indole

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ABSTRACT:-
Indole is a trivial name of benzopyrrole in which 2 and 3 carbon atoms of the nitrogen ring are members of a benzenoidnucleus .Indole is a planar molecule with 10 electrons. It's resonance energy is 47-49 K cal/mole. It is a very weak base with pKa value 3.63. The electrophilic attack results at 3rd position because Presence of high electron density at 3rd position. It has been also supported by the calculation of electron density and by molecular orbital method.

KEY WORDS: Indole, Acetic acid, Methanol.

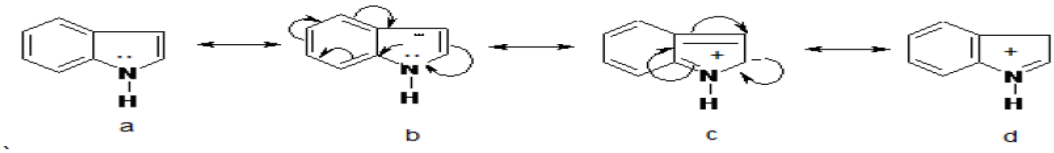
INTRODUCTION

Indole chemistry began to develop with the study of the dye indigo. The word Indole is coined from the word India, a blue dye imported from India known as Indigo. Indigo can be converted to isatin and then to oxindole. Then, in 1866, Adolf von Baeyer reduced oxindole to indole using zinc dust. In 1869; he proposed a formula for indole:

Indole is non-basic nitrogenous compound in which a benzene ring and a pyrrole nucleus are fused in 2, 3 positions of the pyrrole ring. It is aromatic heterocyclic organic compound. It has a bicyclic structure. Indole is colorless crystalline solid and melts at 52'C, soluble in alcohol, benzene and ether. It may be recrystallized from water. [1]

Indole is a trivial name of benzopyrrole in which 2 and 3 carbon atoms of the nitrogen ring are members of a benzenoidnucleus .Indole is a planar molecule with 10 electrons. It's resonance energy is 47-49 K cal/mole. It is a very weak base with pKa value 3.63. The electrophilic attack results at 3rd position because Presence of high electron density at 3rd position. It has been also supported by the calculation of electron density and by molecular orbital method.

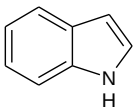
1.1Resonance in indole molecule:-



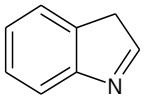
It undergoes all types of reactions for example: Protonation, nitration, sulfonation, acylation, halogenations, and formation of various metal complexes etc. it gives electrophilic as well as nucleophilic reactions. Indoles are probably the most widelydistributed heterocyclic compound in nature. Tryptophan and essential amino acid assuchisconstituentofmostproteins.[11]

Indole is a basic functional unit in plants as well as animals. It can be produced by bacteria as a degradation product of the amino acid tryptophan. It is found in jasmine and in certain citrus plant. Indole is a popular component of fragrances and the precursor to many pharmaceuticals. At very low concentrations, however, it has a flowery smell, and is a constituent of many flower scents (such as orange blossoms) and perfumes. Indole and homologous of indole have been found in coal tar and in molasses tar. It is also found in liver, pancreas, brain and bile. Indole accompanied by its β-methyl homologue, skatole, is found in the feces of human, animal and in the content of intestine. Compounds that contain an indole ring are called indoles. [1]

As isomer of indole in which the nitrogen atom takes part in the double bond is termed 3- pseudoindole or indolenin (1.2) and 2, 3 saturated compounds are known as indoline (1.3).



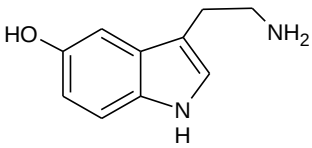
Indole (1.1)



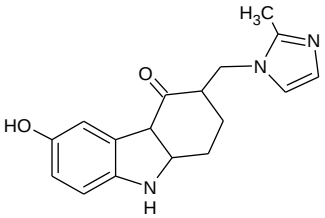
indolenin (1.2)

There are some other oxygenated derivatives of indole are: oxindole (1.4), indoxyl (1.5), dioxindole (1.6) and indole 2, 3-dione or isatin (1.7).

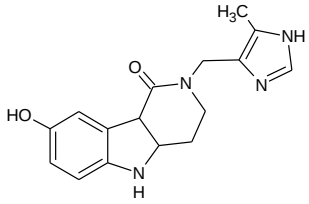
Indole derivatives derived from animals are serotonins (5-HT) and melatonin. Some widely used derivatives are ondansetron for the suppression of nausea and alosteron for treatment of irritable bowel syndrome.



Serotonin (1.8)

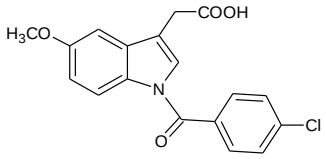


Ondensterone (1.9)



Alosetron (1.10)

From plant, tryptophan derived substances are also useful. Vincristine, an indole alkaloid is still extremely important in treatment of cancer. Brassinin, isolated from turnips is a phytoalexin. It prevents plants from microbial attack. [2] Indole moiety shows various biological activities like antimicrobial, CNS depressant, anti-HIV, anti-inflammatory, analgesic and many other activities e.g. indomethacin (1.11) is useful in treatment of rheumatoid arthritis, explains why indole and its derivatives are still a very interesting molecule since its synthesis in 1866



Indomethacin (1.11)

V. A. Arun Kumar1 ***et. al***. In Silico Analysis of Indoles Against 1KE8 Inhibitors Using Autodock. 1KE8 is known as a potential target for anti-cancer medication. Indoles are biologically active nitrogen heterocyclics known for broad spectrum activities. Modification of Indole ring system with selected structural descriptors has offered a high degree of stereo specificity and diversity in activity to the moiety.[3]

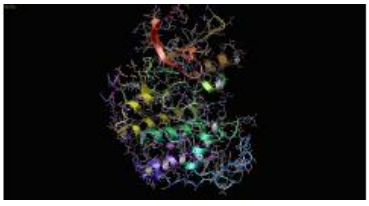
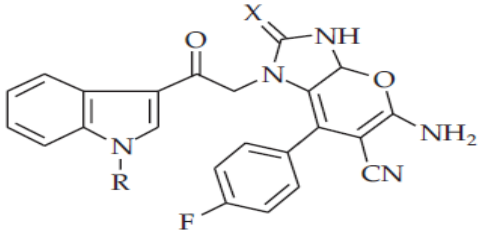


Fig: 3D-structure of 1KE8

Eslam Reda El-Sawy ***et. al.*** Synthesis and biological activity of some new 1-benzyl and 1-benzoyl-3-heterocyclic indole derivatives -Starting from 1-benzyl- (**2a**) and 1-benzoyl-3-bromoacetyl indoles (**2b**) new heterocyclic, 2-thioxoimidazolidine (**4a,b**), imidazolidine-2,4-dione (**5a,b**), pyrano(2,3-*d*)imidazole (**8a,b** and **9a,b**), 2-substituted quinoxaline (**11a,b–17a,b**) and triazolo(4,3-*a*)quinoxaline derivatives (**18a,b** and **19a,b**) were synthesized and evaluated for their antimicrobial and anticancer activities. Antimicrobial activity screening performed with concentrations of 0.88, 0.44 and 0.22 mg mm–2 showed that 3-(1-substituted indol-3- -yl)quinoxalin-2(1*H*)ones (**11a,b)** and 2-(4-methyl piperazin- 1-yl)-3-(1-substituted indol-3-yl) quinoxalines (**15a,b**) were the most active of all the tested compounds towards *P. aeruginosa, B. cereus* and *S. aureus* compared to the reference drugs cefotaxime and piperacillin, while 2-chloro-3-(1-substituted indol-3 yl)quinoxalines (**12a,b**) were the most active against *C. albicans* compared to the reference drug nystatin. On the other hand, 2-chloro-3- -(1-benzyl indol-3-yl) quinoxaline **12a** display potent efficacy against ovarian cancer xenografts in nude mice with tumor growth suppression of 100.0 ± 0.3 %. [4]

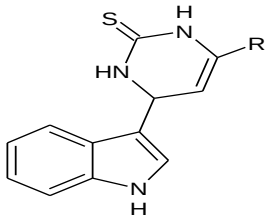


Comp. code	R	X	Comp. code	R	X
6a	CH_2ph	S	8a	CH_2ph	S
6b	COph	S	8b	COph	S
7a	CH_2ph	O	9a	CH_2ph	O
7b	COph	O	9b	COph	O

Srivastava***et.al*** (2011) the indole is found to be a very versatile nucleus in the pharmaceutical field. Indole derivatives are found to contain several biological activities those including antimicrobial, antibiotic, anti-inflammatory, analgesic, anticonvulsant, antimalarial, anticancer, antiulcer, &Antileishmanial, contraceptive, antioxidant etc.[5]

Some synthetic indole derivatives which are used:

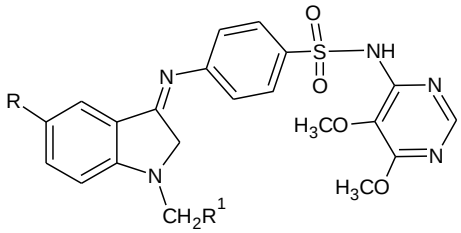
Amir ***et.al*** *(2011)* synthesize 3-substituted indole derivatives with pyrimidine ring and chang the substituent at 6th position of this ring and screened for the biological activities. He found that 4-(1*H*-indol-3-yl)-6-phenyl-1, 2, 3, 4- tetrahydropyrimidin-2-ones/thiones is a potent anti-inflammatory agents.[6]



(2.1)

R= Phenyl, 4-chloro phenyl, 2,4-dichloro phenyl,4-methyl phenyl and 3,4- Dimethyl Phenyl.

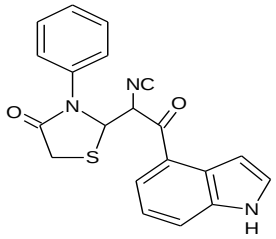
Pandeya S.N. ***et.al*** (2011) synthesized Schiff bases of isatin and 5-methyl isatin with sulphadoxine. The piperidino methyl compounds (2) were found to be the most active anti microbial agent.[7]



(2.2)

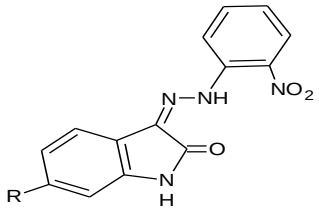
R= H, CH_3 ,R'=$N(CH_3)_2$, $N(C_2H_5)_2$, 1-piperidyl , 4-morpholinyl.

Radwan***et.al*** (2010) synthesized and evaluated the analgesic activity of 3, 4substituted indole derivatives. He prepare various derivatives of indole with various substituent at 3rd and 4th position .from all this compounds, Tholidine-4-one derivative was found to exhibit more analgesic activity than other substituents.[8]



(2.3)

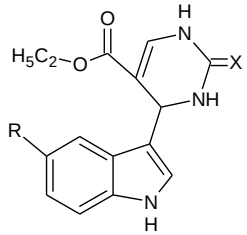
Popp and Pajouhesh***et.al*** (2011) synthesized 3-*o*-nitrophenyl hydrazones of isatin by condensation of isatin with *o*-nitrophenyl hydrazine. These compounds were found to be active intramuscularly against Walker carcinoma-256 and inactive against L-1210 lymphoid leukemia.[9]



(2.4)

R= H, CH3, CF3, COCH3, Br, Cl, SO3H

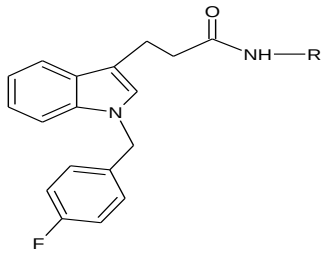
L. C. Heda, rashmisharma et al.Synthesis and Antimicrobial Activity of Some Derivatives of 5-Substituted IndoleDihydropyrimidines- P. Biginelli reported the synthesis of functionalized 3, 4 dihydropyrimidine- 2 (1 H)-ones via three component condensation of an aromatic aldehyde, urea and ethylacetoacetate. This multicomponent reaction is of much importance due to excellent pharmacological properties of dihydropyrimidines. In this account, we synthesized some halo substituted indoledihydropyrimidines and evaluated their antimicrobial activity. The minimum inhibitory concentration (MIC) was determined by micro dilution technique in Mueller-Hinton broth. The MICs were recorded after 24 hours of incubation at 37 0C. These results are promising, showing these compounds are biologically active.[10]



R= H, Cl, Br, I X= O, S

SüreyyaÖlgena,NurtenAltanlarb **et. al.** Antimicrobial and Antiviral Screening of Novel IndoleCarboxamide and Propanamide Derivatives-A few series of indole derivatives were screened for antimicrobial, antifungal and anti-HBV activities. The compounds were tested for their *in vitro* antibacterial activity against*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and for their antifungal activityagainst*Candida albicans*using a disc diffusion method, which measures the diameter of theinhibition zone around a paper disc soaked in a solution of the test compounds. The antimicrobialactivity results showed that

all compounds are as a active as the standard compoundampicillin against *Staphylococcus aureus*.[11]



R= 4-Cl-phenyl, 4-F-phenyl, 2,4-Cl-phenyl

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