Microwave Assisted Synthesis and Biological Activity of Some Novel Indole Derivatives: A Review

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ABSTRACT

Indole and its derivatives have occupied a unique place in the chemistry of nitrogen heterocyclic compounds. The indole derivatives were known for their dying properties[1,2]. Many compounds of indole derivatives having the Structural resemblances to the ancient dye indigo are known in the literature. A Large number of naturally occurring compounds, like alkaloids, were found to Possess indole nucleus[3]. The recognition of the plant growth hormone, heteroauxin, the important amino acids, tryptamine & tryptophan, anti-inflammatory Drug, indomethacine and anticancer drug, indole derivative are the important derivatives of indole which have added stimulus to this research Work.

Key Words: Indole, anti-inflammatory, anticancer drug.

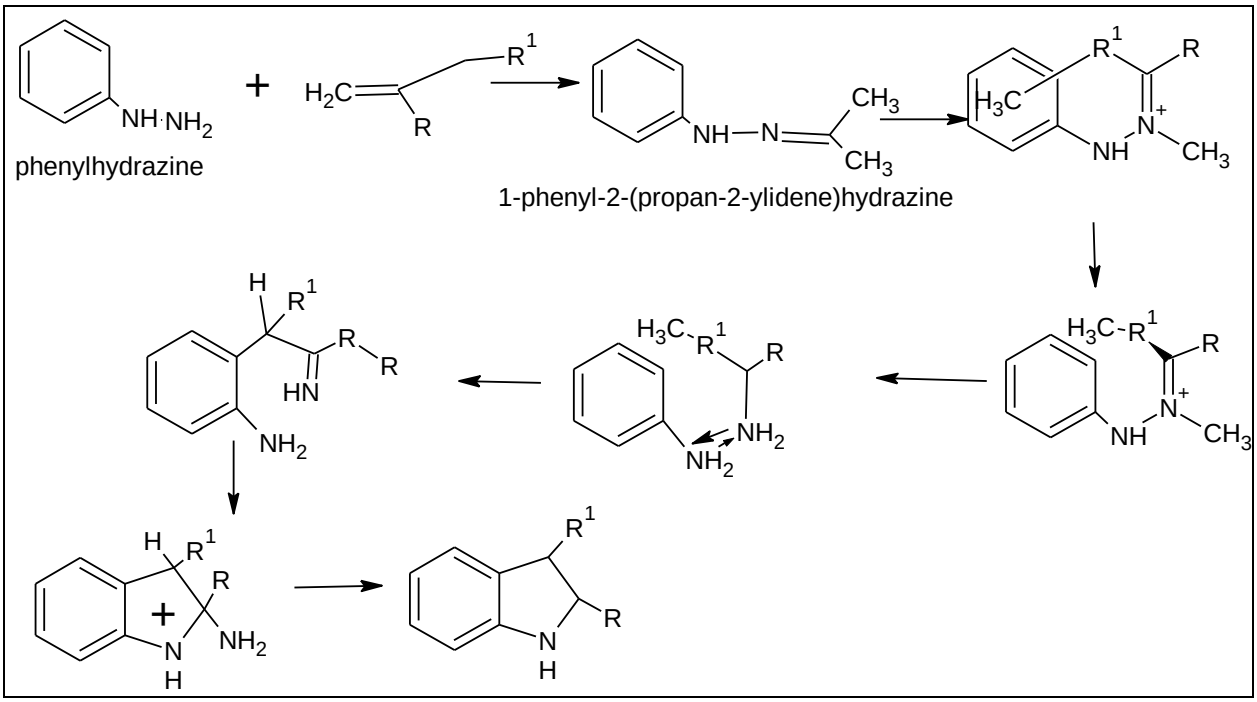
INTRODUCTION

Indole is an aromatic heterocyclic organic compound with formula C_8H_7N. It has a bicycle structure, consisting of a six-member benzene ring fused to a five-member pyrrole ring[4,5]. The amino acid tryptophan is an indole derivative and the precursor of the neurotransmitter serotonin.

FISCHER INDOLE SYNTHESIS[6,7]:

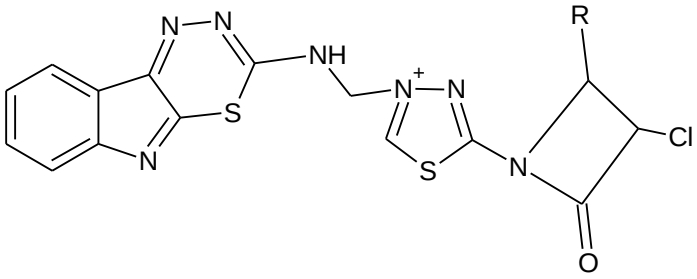
The Fischer indole synthesis is an organic reaction used to convert a phenyl hydrazine and an aldehyde or ketone to an indole using an acid catalyst. The mechanism begins with formation of a phenylhydrazone through the acid catalyzed reaction of the hydrazine with the carbonyl. The phenylhydrazone then rearranges to the enamine and gets protonated on the phenyl nitrogen. An "ene reaction" (3, 3-sigmatropic rearrangement) ensues, resulting in a diimine and loss of aromaticity. Additional key steps include aromatization, formation of a cyclic amine, and the expulsion of ammonia to give the indole product.

MECHANISM OF FISCHER INDOLE SYNTHESIS[8,9,10]:



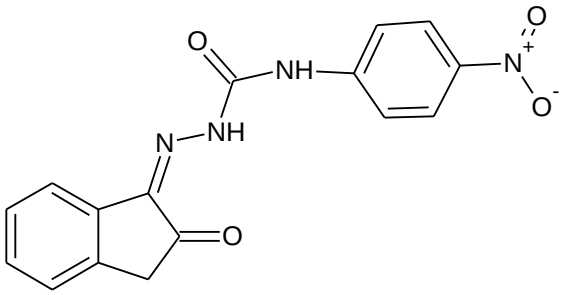
ANTI-INFLAMMATORY ACTIVITY[11]:

Kumar et al synthesized a series of new substituted azetidinoyl and thiazolidinoyl1,3, 4-thiadiazino (6,5-b) indoles and tested for anti inflammatory activities Anti-inflammatory against carrageen an induced rat's paw edema.



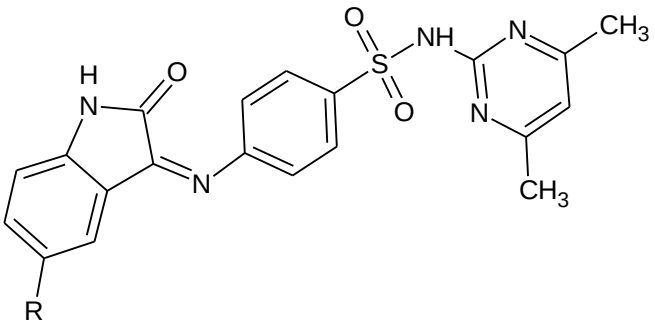
ANTICONVULSANT ACTIVITY[12]: ™

Pandeya et al synthesized a series of p-nitro phenyl substituted semicarbazones and their anticonvulsant activities were screened against maximal electroshock (MES), subcutaneous pentylenetetrazole (scPTZ) and subcutaneous strychnine (scSTY) tests.



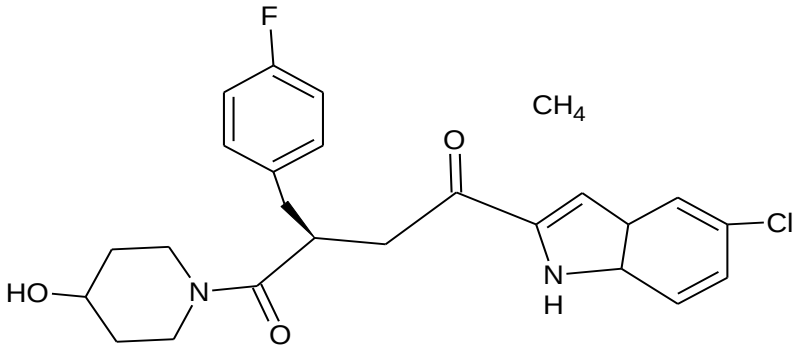
ANTIVIRAL ACTIVITY[13]:

Selvam et al prepared 4-[(1, 2-dihydro-2-oxo-3H-indol-3-ylidene)amino]-N-(4,6dimethyl-2-pyrimidin-2-yl)benzenesulphonamide and its derivatives. The related compounds were tested for antiviral activity against influenza A (H1N1, H3N2, and H5N1) and B viruses in Madin Darby canine kidney (MDCK) cell culture.



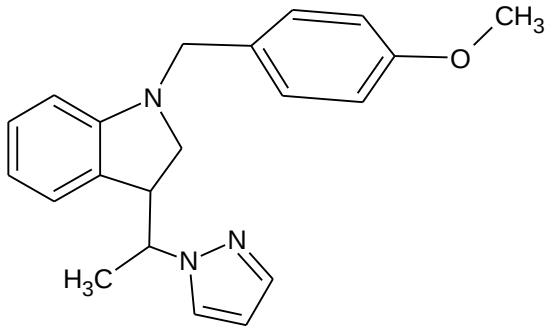
ANTIDIABETIC ACTIVITY[14]:

A distinct site at the monomer interface known as the indole inhibitor site. Compound inhibited liver and muscle GP in the nM range in enzyme kinetics and was active in forskolin-induced, cell-based glycogenolysis in the mM range (1.9 mM).



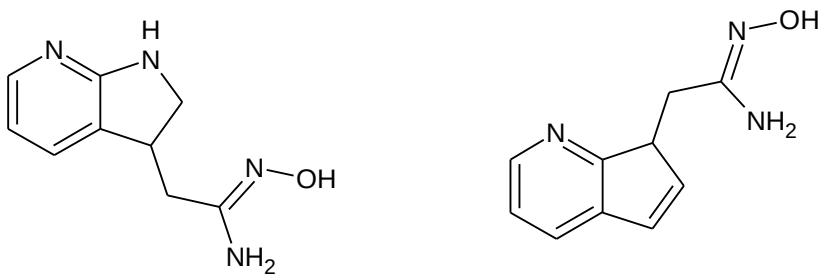
ANTITUMOR ACTIVITY[15]:

Farghaly AR synthesized a series of novel [1-(4-methoxybenzyl)indol-3-yl](1H-pyrazol-1yl)methanones and 1-(1-(4-methoxybenzyl)-1H-indole-3-carbonyl)-3-subsituted-1H-pyrazol-5(4H)-one derivatives and all synthesized target compounds were tested in vitro for antitumor activity using the Alamar Blue assay on a panel of five human tumor cell lines. The cytotoxicity was evaluated on five different cell lines, cervix cancer (KB/HELA), ovarian carcinoma (SKOV-3), brain cancer (SF-268), nonsmall-cell lung cancer (NCl-H460) and adenocarcinoma colon cancer (RKOP-27) and it was observed that these compounds had shown prominent antitumor activity.



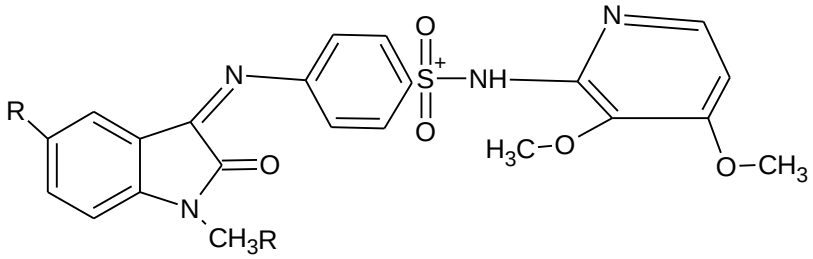
ANTIMICROBIAL ACTIVITY[16]:

Mehta DS et al synthesized a series of novel 1-aryl-2-methyl-3-carboethoxy-5-hydorxy indole derivatives and evaluated their antimicrobial activity against B. mega , B. subtilis bacteria.



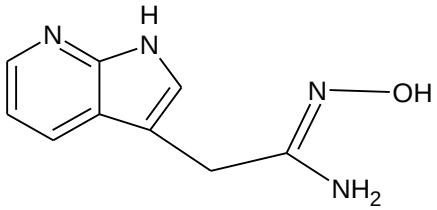
ANTIFUNGAL ACTIVITY[17]:

Pandeya et al synthesized schiff bases of isatin and 5-methyl isatin with sulphadoxine and were evaluated for their in vitro antifungal activity against various fungal strains viz. Candida albicans, Candida neoformis, Histoplasma capsulatum, Microsporum audounii and Trichophyton mentagrophytes. It was found that the piperidino methyl compounds have shown prominent antifungal activity.



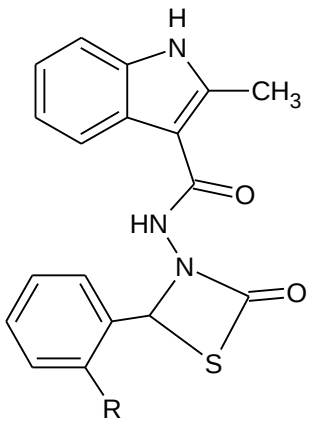
ANTIHYPERTENSIVE ACTIVITY[18]:

Bell MR et al synthesized a series of novel 7-azaindole-3-acetamidoxime and 7-azaindole-1acetamidoxime and evaluated for its antihypertensive activity. These compounds have shown prominent antihypertensive properties.

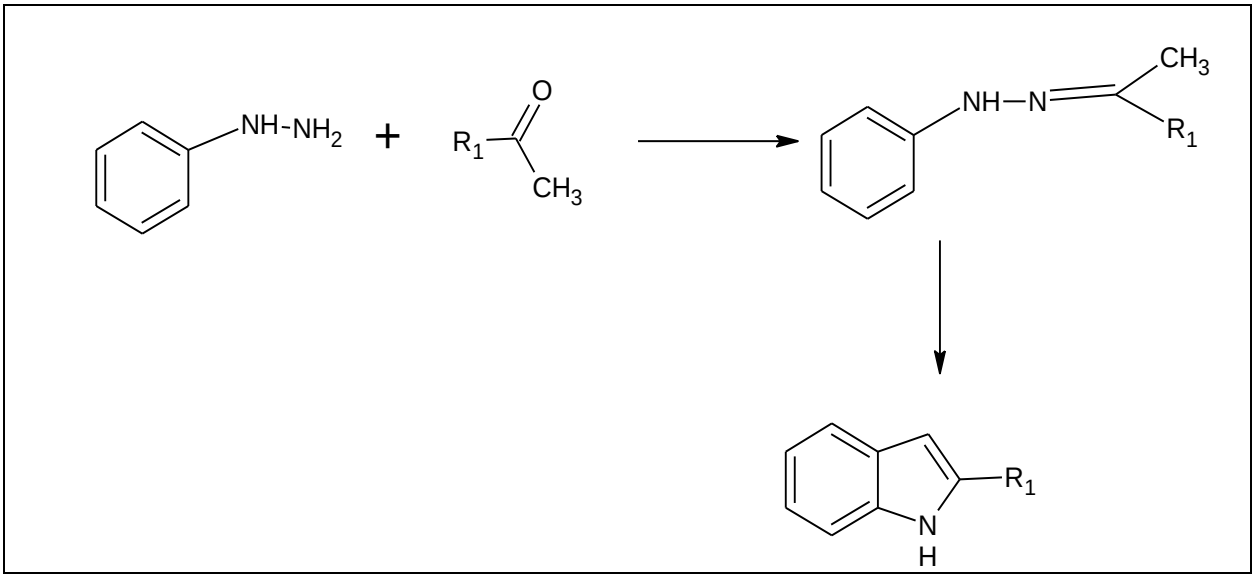


ANALGESIC ACTIVITY[18,19]:

Rapolu Manish et al synthesized a series of novel 2-methyl-1H-indole-3-carboxylic acid[2-(2substitutedphenyl)-4-oxo-thiazolidin-3-yl]amide derivatives and evaluated for their analgesic activity by using hot plate latency and acetic acid induced writhing test. Most of the compounds which are having two hydroxyl group and one methoxy group on the phenyl ring had shown excellent analgesic activity.



METHOD OF SYNTHESIS[20,21]:



In this synthesis addition reaction between Phenyl hydrazine with aldehyde or kectone to convert phenyl hydrazones then again cyclization to form indole product

CONCLUSIONS:

Indole is associated with several biological activities and versatile biological properties of indole derivatives. They are of great interest to the research community. In particular, their physiological, bacteriostatic, antitumor, antioxidant and anti inflammatory, anticonvulsant, antihypertensive, analgesic activities makes these compounds attractive candidates not only for the microbe borne diseases but also for the several other conditions like Alzheimer's disease and others where oxidative stress and inflammation is involved[21]. This review has presented comprehensive details of indole analogues, potent compounds reported for particular biological activity. More research must be carried out to evaluate the therapeutic efficacy of indole derivatives for many other untreatable diseases like AIDS, hepatitis and cancer**.**

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