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Review Article

IMPORTANCE OF PYRAZOLE MOIETY IN THE FIELD OF CANCER

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ABSTRACT

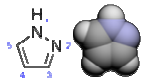
The pyrazole nucleus is found to be very important in the field of pharmacy as well as to develop newer anticancer agent. In the present review our main interest is to emphasize the various synthetic molecules developed to promote the pyrazole molecule in the modern era of anticancer agent.

Keywords: Pyrazole, Cancer, A549, Cytotoxic Activity, Antiproliferative Activity.

INTRODUCTION

Pyrazole

Pyrazole refers both to the class of simple aromatic ring organic compounds of the heterocyclic diazole series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions, and to the unsubstituted parent compound [1].



Iupac Name: Pyrazole

Properties

Molecular formula :	$C_3H_4N_2$
Molar mass:	68.08 mol^{-1}
Melting point:	66-70°C
Boiling point:	186-188°C
Acidity (pKa):	14.0

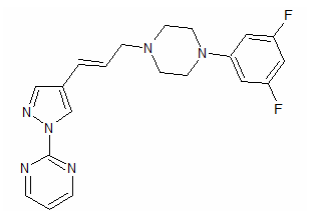
Many substituted pyrazole derivatives are acknowledged to possess a wide range of bioactivities as antimicrobial [2], antitubercular [3], anti-inflammatory [4]. The pyrazole motif makes up the core structure of numerous biologically active compounds. Thus, some representatives of this heterocycle exhibit anti-viral/anti-tumor, antibacterial, analgesic, fungistatic, and anti-hyperglycemic activity [5]. In these review our main intention is to emphasize the role of pyrazole moiety in the cancer.

PYRAZOLE IN CANCER

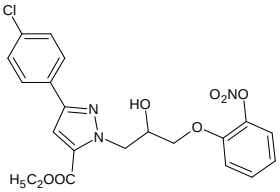
PYRAZOLE AGAINST LUNG CELL CARCINOMA (A549)

There are various pyrazole derivatives are developed by linking pyrimidine, carboxyhydrazide as well as ferrocenyl molecule with the pyrazole cap and all are especially effective against lungs cell carcinoma (A549).

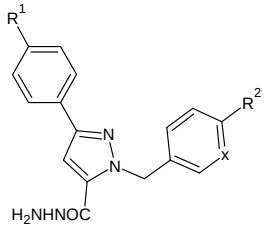
Hitoshi et al prepared Pyrimidinyl pyrazole derivatives as a new scaffold of an anti-tumor agent, which also showed antiproliferative activity against human lung cancer cell lines and inhibited tubulin polymerization [6].



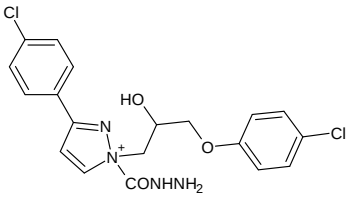
Wei et al synthesized a series of novel small molecules, ethyl 1-(20-hydroxy-30-aroxypropyl)-3-aryl-1H-pyrazole-5-carboxylate derivative which has its potency to suppress A549 lung cancer cell growth [7].



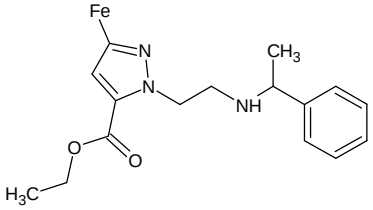
Xia et al synthesized a series of novel 1-arylmethyl-3-aryl-1H-pyrazole-5-carbohydrazide derivative which had inhibitory effects on the growth of A549 cells and induced the cell apoptosis [8].



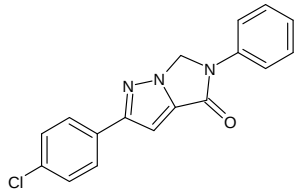
Fan et al synthesized a series of novel 1-(20-hydroxy-30-aroxypropyl)-3-aryl-1H-pyrazole-5-carbohydrazide derivatives could inhibit the growth of A549 cells [9].



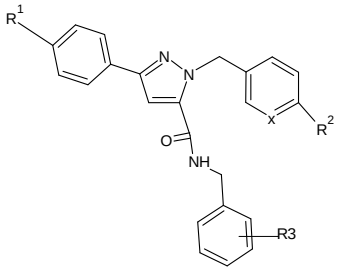
Xie et al synthesized a series of novel 5-alkyl-2-ferrocenyl-6,7-dihydropyrazolo[1,5-a]pyrazin-4(5H)-one derivatives had almost inhibitory effects on the growth of A549 cells [10].



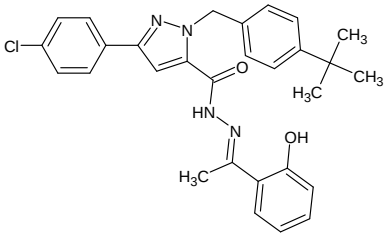
Zhang et al synthesized a series of novel pyrazolo[1,5-a]pyrazin-4(5H)-one derivatives showed that the compounds could inhibit the growth of A549 cells in dosage- and time-dependent manners [11].



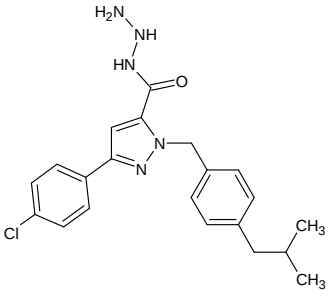
Ding et al synthesized a series of novel 3-aryl-1-arylmethyl-1H-pyrazole-5-carboxamide derivatives which could suppress A549 lung cancer cell growth [12].



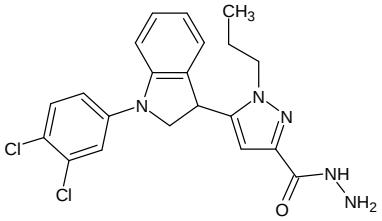
Zheng et al synthesized a series of novel 3-aryl-1-(4-tert-butylbenzyl)-1H-pyrazole-5-carbohydrazide hydrazone derivatives were and investigated the effects of all the compounds on A549 cell growth [13].



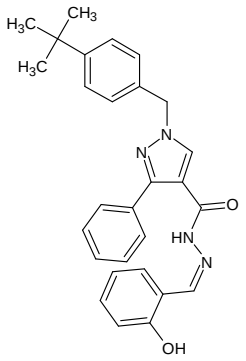
Lian et al synthesized a series of novel 3-aryl-1-arylmethyl-1H-pyrazole-5-carbohydrazide N-b-glycoside derivatives showed inhibitory effects on the growth of A549 lung cancer cells [14].



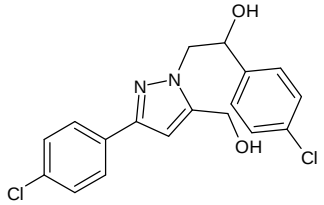
Zheng et al synthesized a series of novel oxime-containing pyrazole derivatives which showed a dose- and time-dependent inhibition of proliferation in A549 lung cancer cell after compound treatment [15].



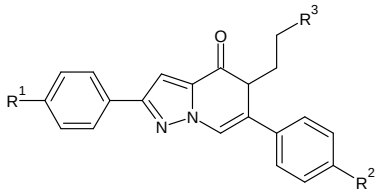
Fan et al developed copper complexes of salicylaldehyde pyrazole hydrazone derivatives (Cu-SPHs) which were stronger growth inhibitors to A549 cells than their corresponding SPHs via inducing apoptosis [16].



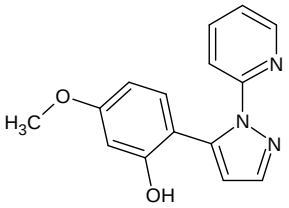
Zheng et al synthesized a series of novel 2-(5-(hydroxymethyl)-3-phenyl-1H-pyrazol-1-yl)-1-phenylethanol derivatives which showed anti-tumour activity by suppressing A549 lung cancer cell growth [17].



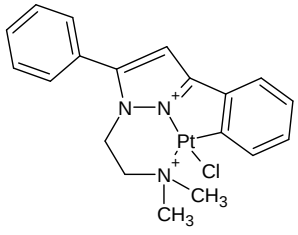
Zheng et al synthesized a series of substituted pyrazolo[1,5-a]pyrazin-4(5H)-one which showed inhibitory action on the growth of A549 and H322 cells in dosage dependent manner [18].



Balbi et al synthesized thirty-six novel pyrazole derivatives and studied their antiproliferative activity in human ovarian adenocarcinoma A2780 cells, human lung carcinoma A549 cells, and murine P388 leukemia cells [19].

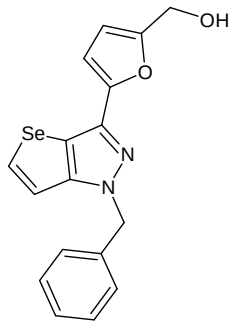


Quirante et al developed platinylated pyrazole moiety active against lung (A549) and breast (MDA MB231 andMCF7) cancer cellular lines [20].

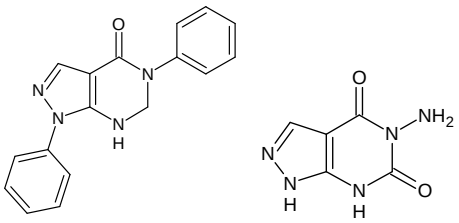


PYRAZOLE MOIETY AGAINST VARIOUS OTHER CELL LINES

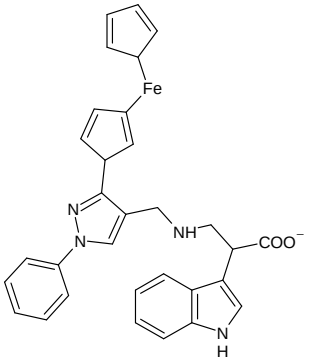
Chou et al synthesized and evaluated 1,3-disubstituted selenolo[3,2-c]pyrazole derivatives were for their cytotoxicity against NCI-H226 non-small cell lung cancer and A-498 renal cancer cell lines [21].



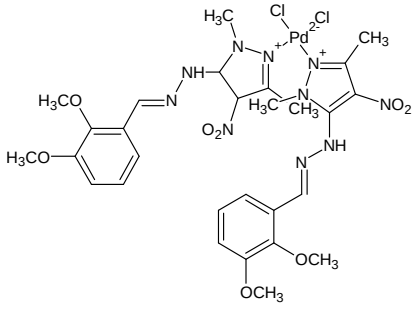
Ghorab et al synthesized a new series of pyrazolo[3,4-d]pyrimidine derivatives and tested for in-vitro anticancer activity against Ehrlich Ascites Carcinoma (EAC) cell line [22].



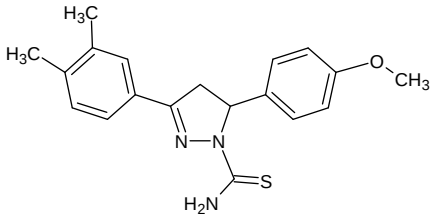
Joksovic et al prepared a series of new N-[(3-ferrocenyl-1-phenylpyrazol-4-yl)methyl]amino acids which showed antitumor activity against cervix adenocarcinoma HeLa, melanoma Fem-x and myelogenous leukemia K562 cell lines [23].



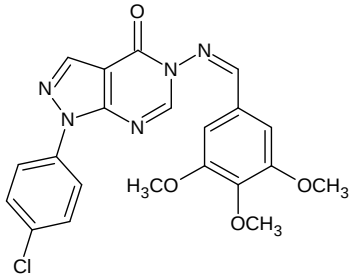
Abu-Surrah et al develop some pyrazole-based trans-palladium(II) complexes trans-[PdCl2(L)2] which has a greater cytotoxic effect of these complexes against the fast growing head and neck squamous carcinoma cells SQ20B and SCC-25 than cisplatin when tested on SQ20B cell line [24].



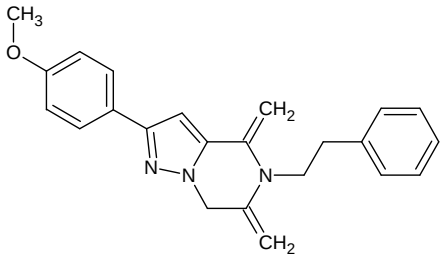
Lv et al develop and synthesized two series of pyrazole derivatives designing for potential EGFR kinase inhibitors as well as antiproliferative activity against MCF-7 with potent inhibitory activity in tumor growth inhibition would be a potential anticancer agent [25].



Hassan et al synthesized new series of pyrazolo[3,4-d]pyrimidines and pyrazole hydrazones and evaluated them for their antiproliferative activity against human breast adenocarcinoma MCF-7 cell line [26].

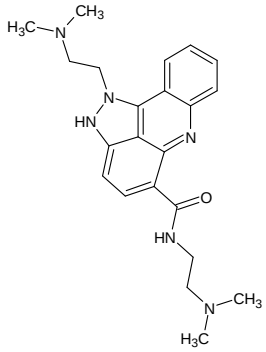


Lv et al Synthesis of 5-benzyl-2-phenylpyrazolo[1,5-a]pyrazin-4,6(5H,7H)-dione derivatives and discovery of an apoptosis inducer for H322 lung cancer cells [27].

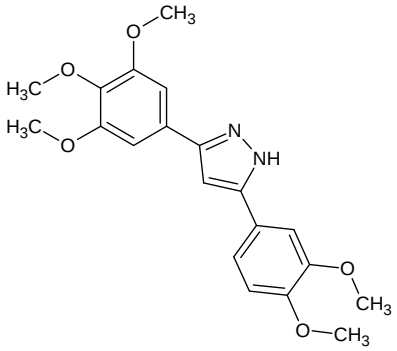


PYRAZOLE MOIETY AS CYTOTOXIC

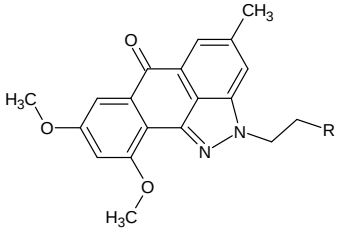
Bu et al prepared pyrazolo[3,4,5-kl]acridines as N-(2-(dimethylamino)ethyl)-1-(2-(dimethylamino)ethyl)-1,2-dihydropyrazolo[3,4,5-kl]acridine-5-carboxamide were found cytotoxic [5].



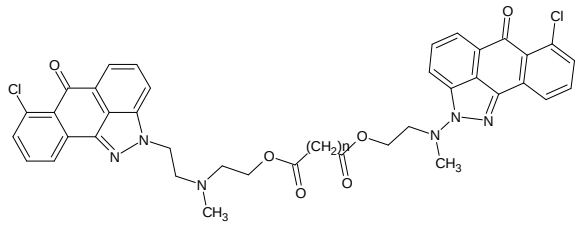
LeBlanc et al synthesized twenty-six epoxide and corresponding pyrazole derivatives, of the structurally related chalcones and combretastatin A-4 and tested them for in vitro cytotoxicity [28].



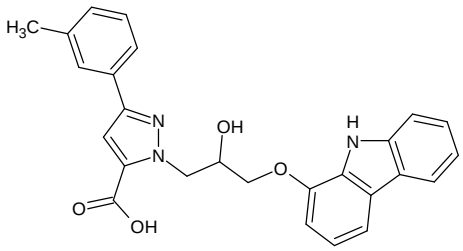
Tan et al derived a series of new anthrapyrazoles from emodin which had more potent cytotoxicity against different tumor cells [29].



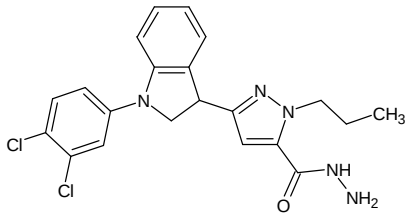
Hasinoff et al designed a series of ester-coupled bisanthrapyrazole derivatives of 7-chloro-2-[2-[(2-hydroxyethyl)methylamino]ethyl]anthra[1,9-cd]pyrazol-6(2H)-one(AP9) and evaluated them by molecular docking techniques in order to find stronger DNA binding and more potent cytotoxic compounds [30].



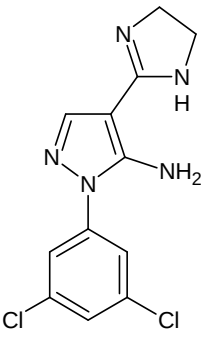
Nagarapu et al synthesized 1-(30-(9H-carbazol-4-yloxy)-20-hydroxypropyl)-3-aryl-1H-pyrazole-5-carboxylic acid derivatives and evaluated in vitro for their cytotoxicity against cancer cells [31].



Zhang et al synthesized a series of novel 3-(1H-indole-3-yl)-1H-pyrazole-5-carbohydrazide derivatives which showed cytotoxic activity [32].

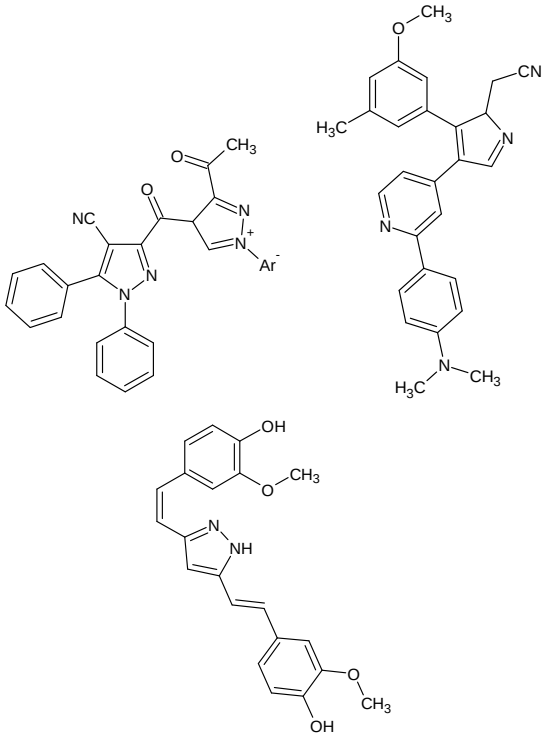


Santos et al synthesized a series of 1-aryl-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazoles and 5-amino-1-aryl-4-(4,5-dihydro-1H-imidazol-2-yl)-1H-pyrazoles the cytotoxicity was assessed [33].

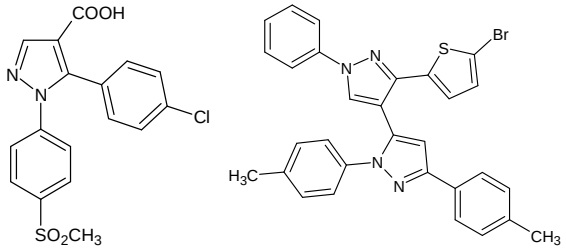


PYRAZOLE MOIETY AS ANTIPROLIFERATIVE AGENT

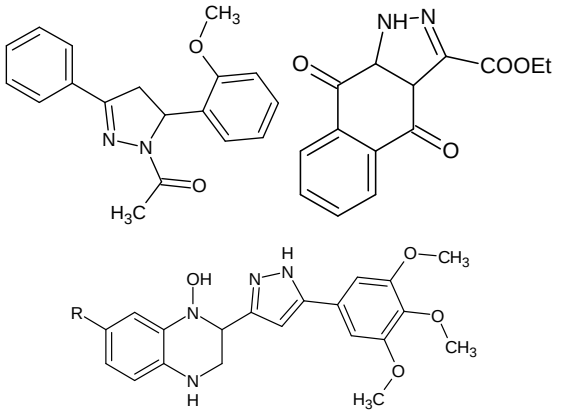
Some pyrazole molecule was also effective as an antiproliferative agent with some dimethylformamid-dimethylacetal (DMF-DMA), as well as FLT3 kinase inhibitor and a protein kinase C inhibitor with intacting the pyrazole scaffold respectively [34, 35, 36].



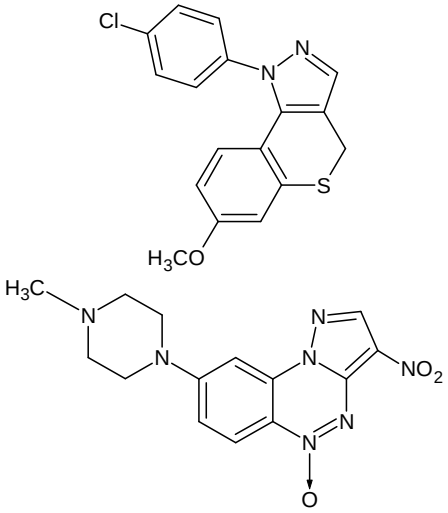
As well as 5-aryl-1-[4-(methylsulfonyl)-phenyl]-1H-pyrazoles and 4-(5-aryl-1H-pyrazol-1-yl)benzenesulfonamides 3, 4, 5, 6, analogues of the COX-2 selective inhibitor and effective against intestinal cancer [37] and a 1H-pyrazolyl derivatives and tested them for their in vivo anti-inflammatory activity [38].



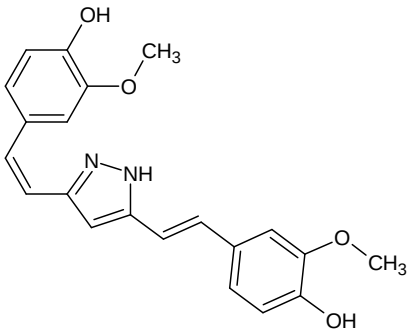
Substituted pyrazolines and 1,4-naphthoquinono [3,2-c]-1H-pyrazoles and their (1,4)-naphthohydroquinone derivatives showed inhibit P-glycoprotein-mediated multidrug resistance and antifungal, antibacterial, and anticancer activities and substituted 3-phenyl-1-(1,4-di-N-oxide quinoxalin-2-yl)-2-propen-1-one derivatives and of their 4,5-dihydro-(1H)-pyrazole analogues inhibit the carrageenin-induced rat paw edema respectively [39, 40, 41].

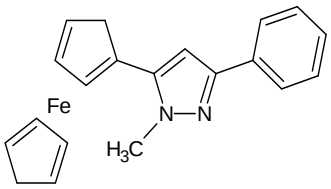


Some novel 1- and 2-phenyl derivatives of the 1,4 dihydrobenzothiopyrano[4,3-c]pyrazole nucleus showed antiproliferative activity [42] and a series of pyrazolo[5,1-c][1,2,4]benzotriazine showed antitumor activity in normoxic and hypoxic conditions respectively [43].

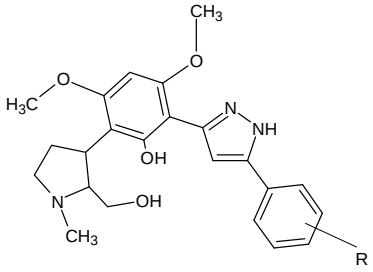


Several isoxazole and pyrazole derivatives of curcumin showed effective interaction with the activator-binding second cysteine-rich C1B subdomain of PKCδ, PKCε and PKCϴ [44] and a ferrocenyl 1,3,5-trisubstituted pyrazoles showed some effective antiproliferative action [45].

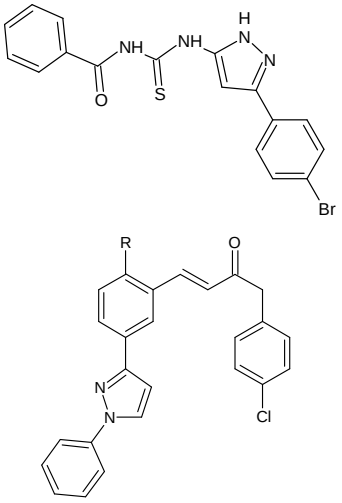




Bandgar et al synthesized a combinatorial library of 3,5-diaryl pyrazole derivatives, all the synthesized compounds were evaluated for their anticancer activity [46].



Nitulescu et al synthesized a series of functionally substituted pyrazole compounds which showed in vitro for their antiproliferative effects [47] and a novel (E)-1-aryl-3-(3-aryl-1-phenyl-1H-pyrazol-4-yl)prop-2-en-1-ones (pyrazolic chalcones) also showed potential anti-tumour activity respectively [48].



CONCLUSION

Pyrazole is a unique molecule in the field of cancer which interacts with various heterocyclic atoms. Not only with heterocyclic rings but also through various inorganic complexes.

So this unique template must act like a boon in the field of developing various synthetic anticancer agents.

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