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Review Article

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REVIEW OF CURRENT ADVANCEMENTS IN THE USE OF PYRAZOLE DERIVATIVES AS ANTICANCER AGENTS IN SEVERAL CELL LINES

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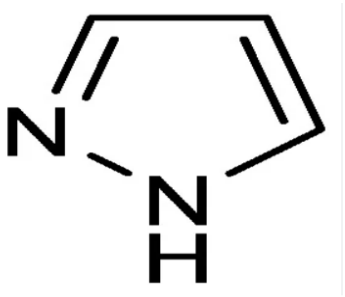
ABSTRACT

It has been discovered that the pyrazole nucleus is crucial for both the development of novel anticancer agents and in the field of pharmacy. Pyrazole is a flexible lead ingredient that can be used to create strong bioactive compounds for drug discovery and development, especially in the treatment of cancer. The different synthetic compounds created to support the pyrazole molecule in the contemporary anticancer agent period are the focus of the current review.

KEYWORDS: Pyrazole, Anticancer, Breast cancer, Colon cancer, Lung cancer, Brain cancer.

INTRODUCTION

Pyrazole, any member of the heterocyclic series of organic compounds with a ring structure made up of three carbon atoms and two nitrogen atoms in close proximity.[1] The molecule with the molecular formula $C_3H_4N_2$ known as pyrazole is the most basic member of the pyrazole family. The 1,3-diketones and hydrazines react to form the pyrazole compounds, which are not known to occur in nature. As medicines and dyes, many synthetic pyrazole chemicals are crucial.[2]

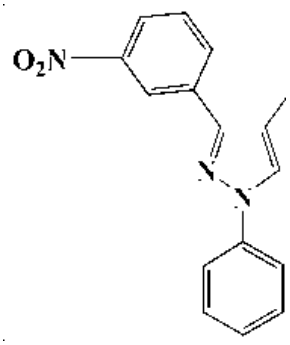


Numerous substituted pyrazole derivatives are known to have a variety of bioactivities, including antibacterial, antitubercular, anti-inflammatory, and etc. Numerous physiologically active chemicals have core structures that contain the pyrazole motif.[3] As a result, several examples of this heterocycle have antiviral/antitumor, antibacterial, analgesic, fungistatic, and antihyperglycemic properties.

The purpose of this work is to present the chemical structures of pyrazole derivatives that have demonstrated anti-cancerous efficacy against a variety of cancer types to date. By allowing chemists and biologists to identify the promising structures, they can direct chemical synthesis to find more potent anticancer drugs.

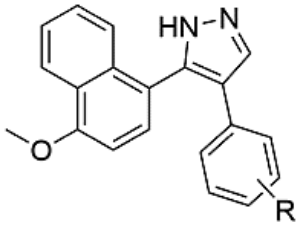
Pyrazole as breast cancer agent

Dina H. Dawood *et al*, synthesised a new set of pyrazoles conjugated with pyrazoline, triazolo-pyrimidine and pyrazolone moieties and investigated for their anticancer efficiency against human breast cancer MCF-7. The effectiveness of the novel analogues' inhibitory activity against VEGFR-2 kinase was further investigated, and the percentage of inhibition ranged from 70–79%. The promising substance 12c caused pre-G1 apoptosis and cell development to stop at the G2/M phase, and it enhanced apoptosis by activating caspase-3 twice.[4]

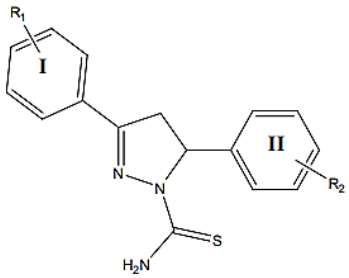


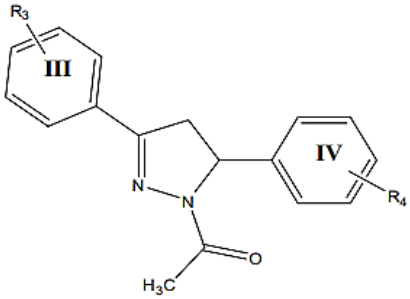
Guangcheng Wang *et al.*, synthesised a new series of pyrazole-naphthalene derivatives and evaluated for their anticancer activity against human breast cancer cell lines (MCF-7). The majority of recently created compounds had strong antiproliferative activity in the IC_{50} range of

2.78 0.24 M to 9.13 0.47 M. Compound compound 5-(4-methoxynaphthalen-1-yl)-4-phenyl-1h-pyrazole derivative, which has ethoxy at the 4-position of the phenyl ring and has an IC_{50} value of 2.78 0.24 M, was discovered to be the most effective of the group, being five times more effective than the benchmark medication cisplatin (IC_{50} = 15.24 1.27 M). Furthermore, the IC_{50} values for compound 5-(4-methoxynaphthalen-1-yl)-4-phenyl-1h-pyrazole derivative and colchicine, which are 4.6 M and 6.7 M, respectively, demonstrated the same capacity to inhibit tubulin polymerization. Studies on the cellular mechanisms revealed that compound 5-(4-methoxynaphthalen-1-yl)-4-phenyl-1h-pyrazole derivative caused apoptosis and stopped the cell cycle at the G2/M phase.[5]

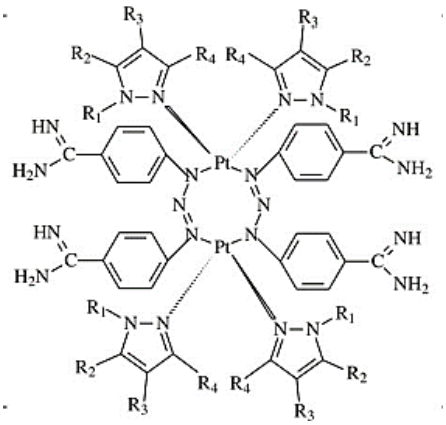


Peng-Cheng Lv *et al.*, many pyrazole compounds that are intended to be potential EGFR kinase inhibitors have been synthesised. It was possible to observe significant EGFR inhibitory effect in some of them. At an IC_{50} of 0.07 lM, which was comparable to the positive control erlotinib, -4, 5-dihydro-1H-pyrazole-1-carbothioamide displayed the most potent EGFR inhibitory activity. Many pyrazole compounds have potent antiproliferative effects against MCF-7, according to the results of antiproliferative assays.[6]

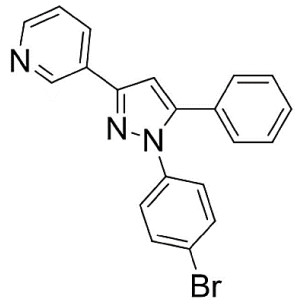




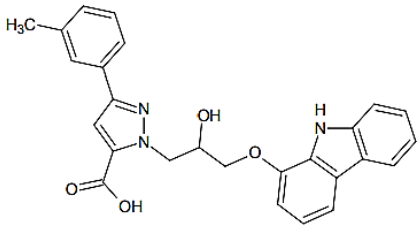
Robert Czarnomysy *et al*., synthesised and characterised six novel compounds of platinum (II) with pyrazole derivatives. Using the MTT test, the cytotoxic activity of these complexes against the breast cancer cell lines MCF-7 and MDA-MB-231 was assessed. The Annexin V-fluorescein isothiocyanate/propidium iodide assay was used to assess the induction of apoptosis. Also, they ascertained how test substances affected the cell cycle and the activity of caspase-3, -8, and -9. Cell imaging supported the discovered caspase activity data. The test results revealed that new pyrazole platinum (II) complexes were more effective at suppressing the growth of two breast cancer cell lines than the standard drug cisplatin.[7]



Hanumappa Ananda *et al.*, synthesised a pyrazole derivative 3-(1-(4-bromophenyl)-5-phenyl-1H-pyrazol-3-yl) pyridine displays significant cytotoxicity against mammary carcinoma cells. By using immunohistochemistry and quantitative RT-PCR to examine ER- expression in living organisms, it was discovered that the substance had an ER- antagonistic effect since it caused tumour cells to express less ER.[8]

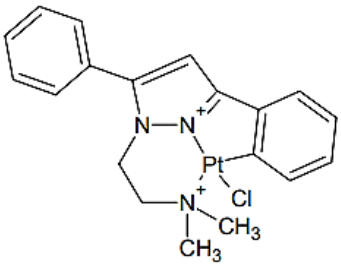


Nagarapu *et al.*, synthesized 1-(30-(9H-carbazol-4-yloxy)-20- hydroxypropyl)-3-aryl-1H-pyrazole-5-carboxylic acid derivatives and evaluated in vitro for their cytotoxicity against cancer cells.[9]

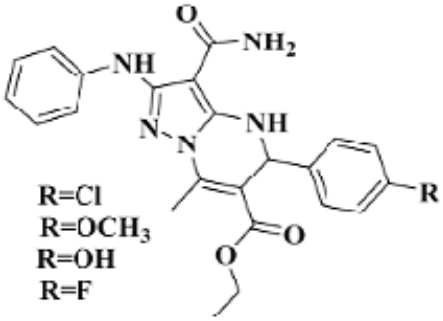


Pyrazole as lung cancer agent: -

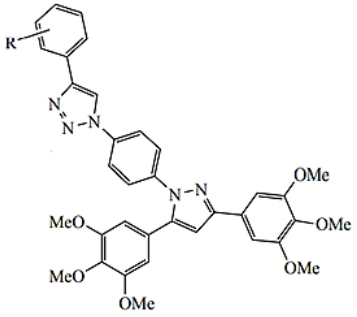
Quirante *et al.*, developed platinylated pyrazole moiety active against lung (A549) and breast (MDA MB231 andMCF7) cancer cellular lines.[10]



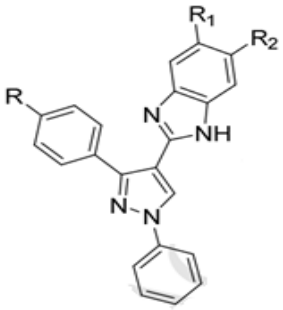
Ghada M.E. Ali *et al.*, synthesised different series of novel pyrazole and pyrazolo[1,5-a] pyrimidine derivatives for their ability to inhibit CDK2/cyclin A2 enzyme in vitro. Cytotoxicity tests were carried out to assess the degree of sensitivity and selectivity of cancer and normal cells to the targeted substances. Four different human tumour cell lines, including the human lung cancer cell line A549, were used to test the anticancer efficacy of all freshly produced compounds.[11]



R. Lakkakula *et al.*, synthesized and evaluated a novel series of 1,2,3-triazole derivatives combined with N-aryl pyrazoles for their anticancer activities against A-549 and another cell line, by using MTT test with doxorubicin as the positive control.[12]

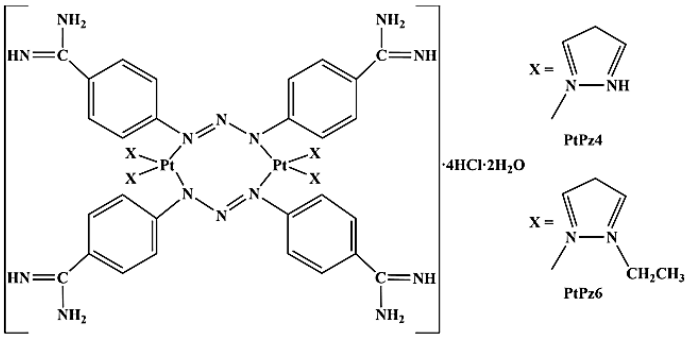


T.Srinivasa Reddy *et al.*, have in order to test their potential antiproliferative effect against three human carcinoma cell lines, including the A549 lung lineage, the researchers created a series of forty distinct benzimidazole hybrids containing pyrazole.[13]



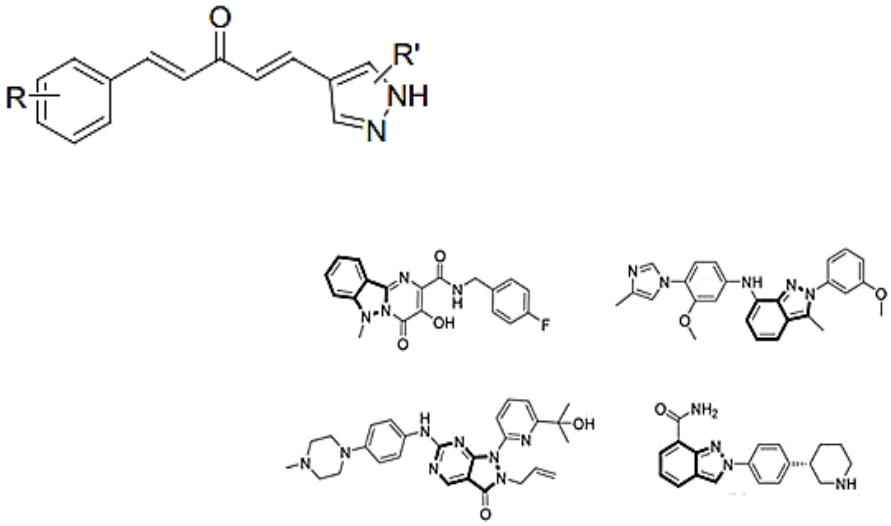
Pyrazole as colon cancer agent:

Katarzyna Supruniuk et al., evaluated the efficacy of cisplatin and its derivatives, anti-MUC1 mAb, two pyrazole-platinum (II) complexes (PtPz4, PtPz6), and cisplatin (cisPt) in monotherapy, as well as mAb coupled with cisplatin and its derivatives.[14]

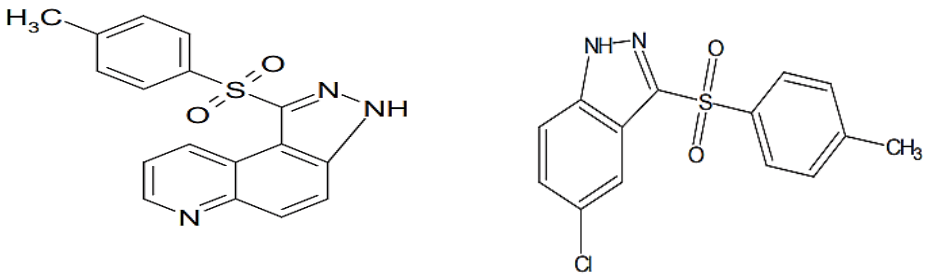


Zhenli Min *et al.*, fifteen compounds were produced, described using spectrum data, and then assessed for cytotoxic activity using the MTT assay against a panel of four human cancer cell lines: gastric (SGC-7901), liver (HepG2), lung (A549), and colon (SW620) cancer cells. [15]

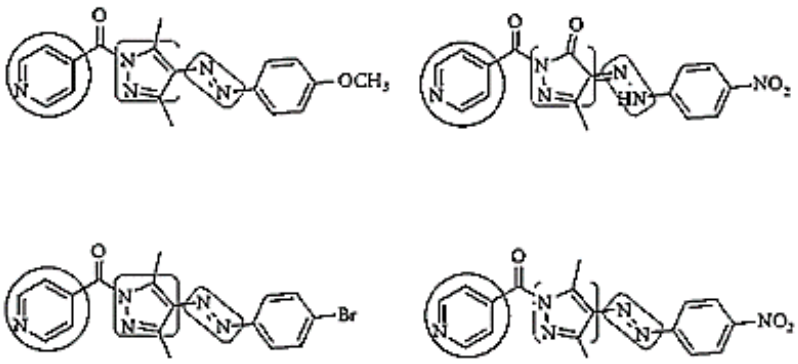
Jia Xu *et al.*, developed a methodology for expeditious access to structurally diverse and complex pyrazole-pyrazines in one-pot. The intramolecular N2-arylation of pyrazoles with allenes at the triple bond's C-position is a unique cascade reaction. The approach for producing bioactive chemicals was tested in the colorectal cancer cell lines HCT116 and SW620, and the results confirmed its viability.[16]



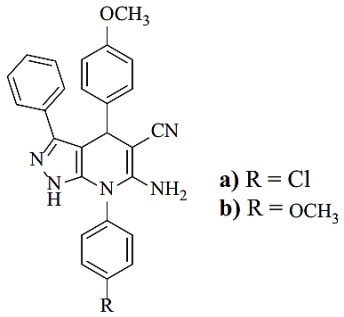
E. Toton *et al.*, synthesised 5-(p-toluenesulfonyl) pyrazolo[4,3-f] quinoline (tospyrquin) and 5-chloro-3-(p-toluenesulfonyl) indazole (tosind), two novel synthetic pyrazoles, were examined for their proapoptotic properties in HT29 colon cancer cells, which exhibit the p53 gene point mutation (G/A in codon 273).[17]



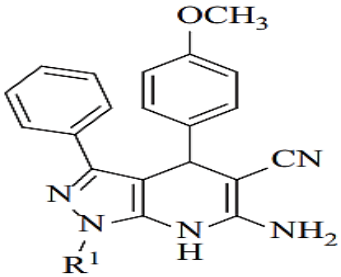
Abdulrhman Alsayari *et al.*, synthesised pyrazole by the appropriate synthetic protocols. A Sulforhodamine B assay against cancer cell lines was used to assess the antiproliferative properties (HCT 116, MCF-7). The mechanism through which pyrazole derivatives produce anticancer effects has been investigated using in vitro and in silico molecular docking experiments with xanthine oxidase.[18]



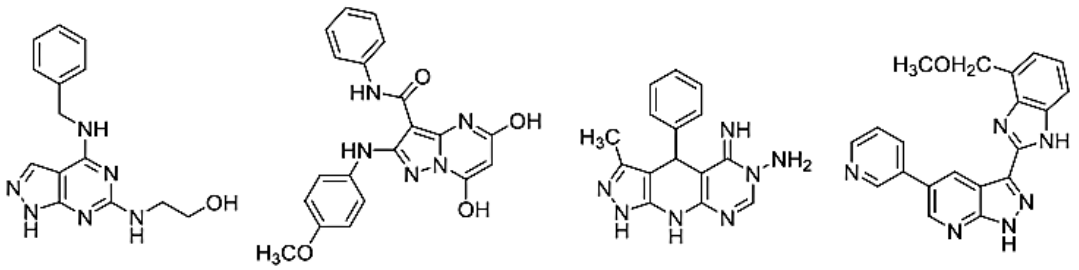
Eissa *et al.*, create new anticancer agents with a series of 1*H*-pyrazolo[3,4-b] pyridine derivatives. 15 substances were tested in vitro for their ability to inhibit the proliferation of the HCT-116 cell line. Also, using the DNA/methyl green test and association constant experiment, the DNA binding affinity of the produced compounds was examined as a probable mechanism for the anticancer activity. The most significant anticancer composite showed good DNA binding affinity comparable to that of doxorubicin and daunorubicin, and the results of the DNA binding assay were consistent with the results of the cytotoxicity test.[19]



a) R = Cl
b) R = OCH_3

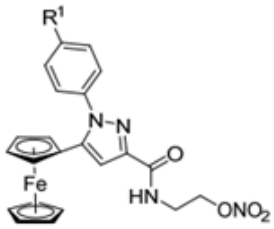


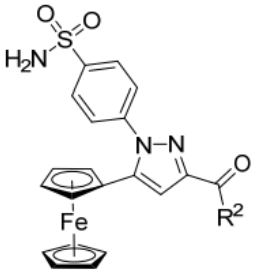
Zahra Kassem *et al.*, aims to create DZ-BAU2021-14N nanocrystals using two different stabilisers and the antisolvent precipitation technique, and to compare their in vitro antiproliferative and cytotoxic effects to free DZ-BAU2021-14 using the MTT assay on the non-tumorigenic NCM-460D and two colorectal cancer cell lines HCT-116 and HT-29. [20]



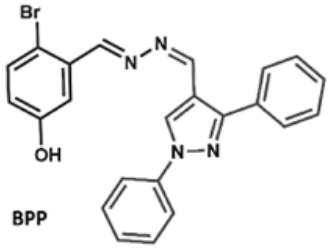
Pyrazole as brain cancer:

Shen-Zhen Ren *et al.*, novel ferrocene-pyrazole compounds with nitric oxide donors were developed, created, and biologically tested as COX-2 inhibitors for cancer treatment.[21]

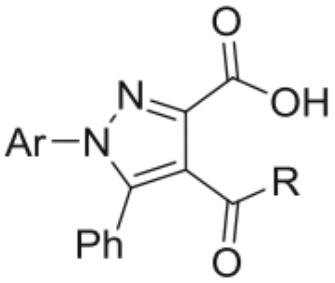




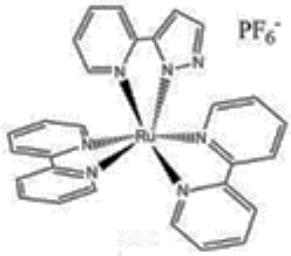
Karuppiah Krishnaveni *et al.*, synthesised a new tripodal, fluorogenic and chromogenic receptor, 5-bromosalicyl hydrazone appended pyrazole. The probe could perhaps serve as a chemical device for the intracellular detection of Zn2+ ions in biological systems, as shown by the findings of the live cell fluorescence imaging examination of the probe BPP in both HeLa cells and Zebrafish embryos.[22]



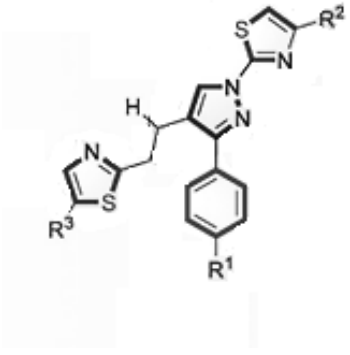
Rahmi Kasımogˇulları *et al.*, novel 4-substituted-1-(3-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid derivatives were synthesized. The antiproliferative effects of synthetic compounds were examined in vitro against the Vero (African green monkey kidney), C6 (rat brain tumour), and HeLa (human uterus carcinoma) cells.[23]



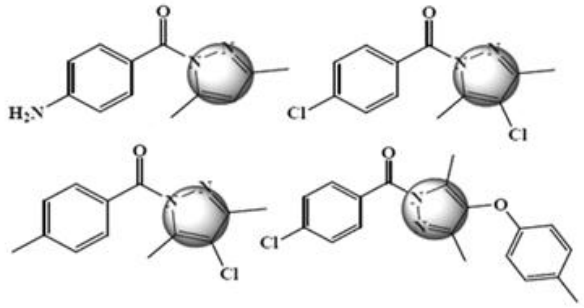
Gao Wen Yang *et al.*, prepared one Ru (II) compound based on 3-(2-pyridyl) pyrazole (Hpypz) and 2,2'-bipyridine. By means of nanoprecipitation in distilled water, this chemical can self-assemble to create nanoparticles (NPs). These NPs exhibit strong phototoxicity in an in vitro investigation using Hela cells, with a low IC_{50} (half-maximal inhibitory dose) of only 8 g/mL (12 M), but no dark toxicity. Furthermore, Hela cell migration can be inhibited by such NPs, suggesting a possibility for interference with the spread of malignancies in vivo.[24]



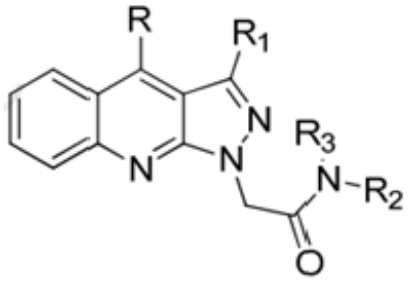
K.K. Bansal *et al.*, synthesised fourteen N-[{(substituted-phenylthiazol-2-yl)-3-aryl-1H-pyrazol-4-yl} methylene]-5-substituted-thiazol-2-amine (5a-n) analogs. Excellent cytotoxicity was demonstrated against MCF-7 and HeLa cells.[25]



Pervaiz Ali Channar *et al.*, synthesised novel aryl pyrazole derivatives using 1, 3-dicarbonyl units then screened for antitumor activity. Four compounds demonstrated the most potent anticancer agent against the HeLa cancer cell line, according to an in vitro anti-cancer study. But the effects of the 4-chlorophenyl substitution were significantly larger than those of the other two substituted chlorinated derivatives. The 4-position of the methyl-substituted derivatives was found to be more advantageous for the HeLa cell line.[26]



G. Jitender Dev *et al.*, synthesized a series of novel 2,3-pyrazole fused quinoline derivatives functionalized with alkylamides. Using the MTT assay and 5-fluorouracil as a reference drug, the compounds were tested for anticancer activity against a number of human cancer cell lines, including Hela (ATCC No. CCL-2).[27]



CONCLUSION

Five-membered nitrogen heterocyclic pyrazole is a common component of many pharmacologically effective substances. The creation of bioactive compounds incorporating heterocyclic pyrazoles has drawn increasing attention. This review emphasised the condition of important portion in the creation and advancement of fresh drug candidates for the treatment of several illnesses in general and cancer in particular.

In light of the foregoing review, it is important to note that research has recently been done on the pyrazole, its derivative, and the hybrid pyrazole to better understand the mechanism of action of this family of drugs. Applications of this family in various cell lines have shown promising results, particularly in breast cancer cell lines, lung cancer cell lines, liver cancer cell lines and brain cancer cell lines. Because this field is seeing an increase in publications, new therapies involving members of this family of heterocycles may be developed in the near future.

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