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Mini review on anticancer activities of Pyrazole Derivatives

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Cancer continues to be a global concern to humanity, posing a threat to both developed and developing countries. Compounds with various heterocyclic moieties have piqued interest in drug development. Oxadiazole is a kind of heterocyclic molecule that has sparked a lot of interest in medicinal chemistry due to their wide spectrum of pharmacological and biological activity [1]. New anti-cancer drugs are being investigated all around the world [2,3]. The majority of new synthetic anti-cancer drugs are heterocyclic derivatives, in which structures having an oxadiazole ring form a class of molecules with very strong cytotoxic potential [4]. Oxadiazoles are heterocyclic compounds with two carbon atoms, two nitrogen atoms, and one oxygen atom which ocscur in many isomeric forms. Regio isomeric forms of oxadiazoles have been expressed in (Figure 1). The presence of the 1,2,4-oxadiazole ring in a molecule impacts its physicochemical and pharmacokinetic characteristics [5]. The oxadiazole ring is a key component of the pharmacophore since it can interact with ligands [6]. Oxadiazole scaffold is a versatile material that has undergone substantial research in recent years. In certain circumstances, it functions as a flat aromatic linker to ensure that the molecule is oriented correctly [7]. The anti-cancer effects of 1,2,4-oxadiazole derivatives appear to be of special relevance, given the ever-increasing prevalence of many forms of cancer [8]. This article comprises 1,2,4-oxadiazole derivatives which showed prominent anticancer activity on different cancer cell lines. 1,2,4-oxadiazole is also a privileged scaffold for Anticancer, Antibacterial [9].

Cancer is still a menace to both industrialised and developing nations, making it a problem for all of humanity. In the field of drug development, compounds having diverse heterocyclic moieties have attracted attention. Due to their broad range of pharmacological and biological action, oxyadiazole is a type of heterocyclic molecule that has generated a great deal of attention in medicinal chemistry [1]. All across the world, new anti-cancer medications are being researched [2,3].

New synthetic anti-cancer medications are typically heterocyclic derivatives, and compounds with an oxadiazole ring belong to a class of chemicals with extremely high cytotoxic potential [4].

There are numerous isomeric forms of oxyadiazoles, which are heterocyclic compounds having two carbon, two nitrogen, and one oxygen atom. Oxadiazoles' regio isomeric forms have been expressed. Any disease that can affect any region of the body is referred to as cancer. Other terminology used are malignant tumours and neoplasms. One characteristic of cancer is the quick development of abnormal cells that grow outside of their normal boundaries, invade nearby body parts, and eventually spread to other organs. This process is known as metastasis. The main reason why cancer patients die is because of widespread metastases. The chemical formula for pyrazole is C3H4N2. It is a heterocyclic organic compound with a ring structure made up of three carbon atoms and two nitrogen atoms in close proximity. The 1H-tautomer of pyrazole is

identified by the abbreviation NCI Thesaurus (NCIt). A pyrazolium's conjugate base. A broad range of illnesses that can affect any region of the body are collectively referred to as cancer. Neoplasms and malignant tumours are other words that are used. One distinguishing characteristic of cancer is the quick development of aberrant cells that quickly outgrow their normal bounds and can infiltrate nearby body sections before metastasizing to other organs. The main factor in cancer deaths is widespread metastases.

Causes:

In a multi-stage process that often goes from a pre-cancerous lesion to a malignant tumour, cancer develops when normal cells undergo a transition into tumour cells. These modifications are the outcome of interactions between a person's genetic factors and three different types of outside forces, such as: Biological carcinogens include infections from specific viruses, bacteria, or parasites. Physical carcinogens include ultraviolet and ionising radiation. Chemical carcinogens include asbestos, tobacco smoke, alcohol, aflatoxin (a food contaminant), and arsenic (a drinking water contaminant). The International Agency for Research on Cancer (IARC), a division of WHO, maintains a classification of cancer-causing substances.

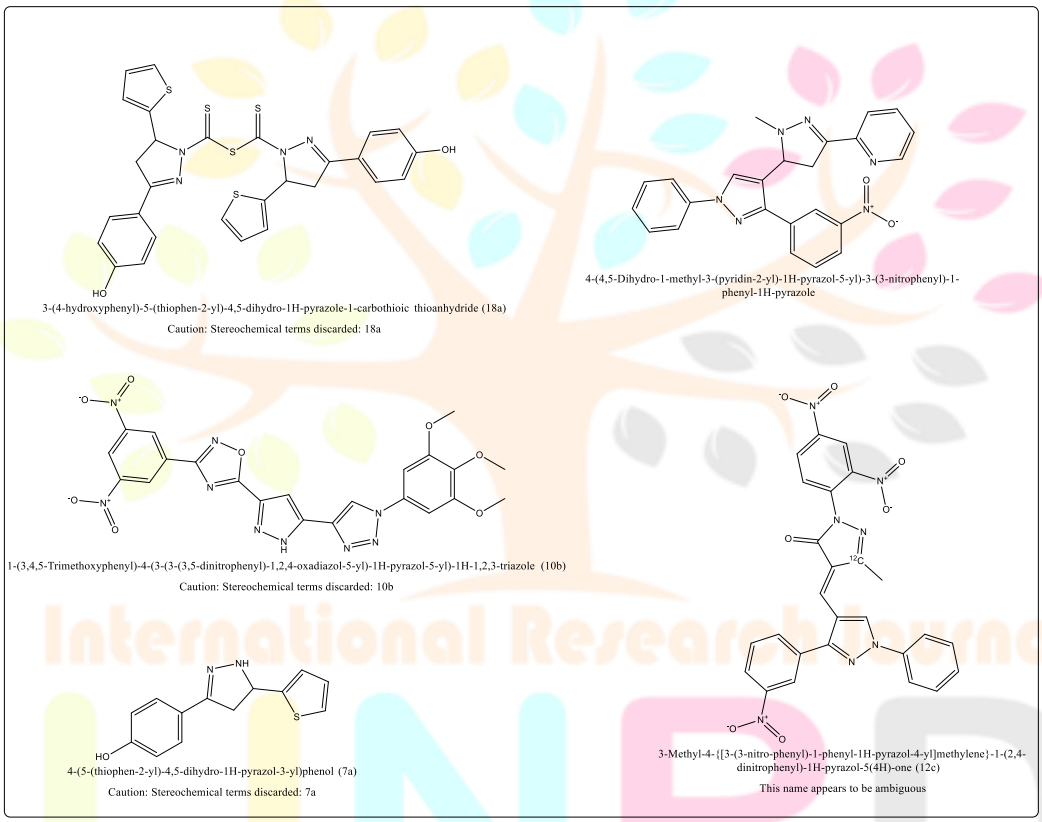
Structure of pyrazole:

Pyrazole belongs to the class of five membered heterocycles, containing two double bonds and two nitrogen atoms at adjacent positions [28]. Pyrazole, a structural isomer of imidazole, is an aromatic molecule. It possesses pyrrole and pyridine like nitrogen atom at 1- and 2- position, unlike imidazole having nitrogen atom at 1- and 3- position. Pyrazole is, therefore, also identified by the name “1,2-diazole” [29]. When pyrazole moiety gets attached to the benzene ring, the resulting nucleus is called “indazole” or “isoindazole” depending upon the position of 2. The pyrazole's structure Pyrazole, which has two double bonds and five members, is a member of the class of heterocycles with five members. neighbouring locations of two nitrogen atoms [28]. A structural isomer of imidazole called pyrazole is a molecule with aroma. It has nitrogen atoms at positions 1 and 2 that are similar to those in pyrrole and pyridine.unlike imidazole, which has nitrogen atoms in positions 1 and 3. Pyrazole is hence also referred to as "1,2-diazole" [29]. When the pyrazole moiety joins the benzene depending on where the centre of the ring is located, the resulting nucleus is known as a "isoindazole" or a "indazole .Pyrazole in cancer management MCF-7 and VEGFR-2 inhibition plays important role. Pyrazoline is combined with pyrazole. Pyrazolone moieties and triazolopyrimidine are synthesis for anticancer activity against MCF-7. 4b compound sensitive toward breast carcinoma. The anti-cancer activity of 4b the pyrazole derivatives in MCF-7 cell line is 26.73(10.65±1.14). Cytometric analysis reveals the compound 12c swift to pre-G1 apoptosis. Pyrazole is an important biological factor that possesses all type of biological activity A-549, MCF-7, HeLA, HepG-2, PaCa-2 and DLD-1 these are six different cell lines viz. (2) The investigated derivatives of exhibited a low HOMO-LUMO energy gap ranging from 2.70 to 2.34 eV, 4c or 4b both and 6b respectively. (3)

Pyrazole is numerous pharmaceutical active compound. Pyrazole is used to treat :

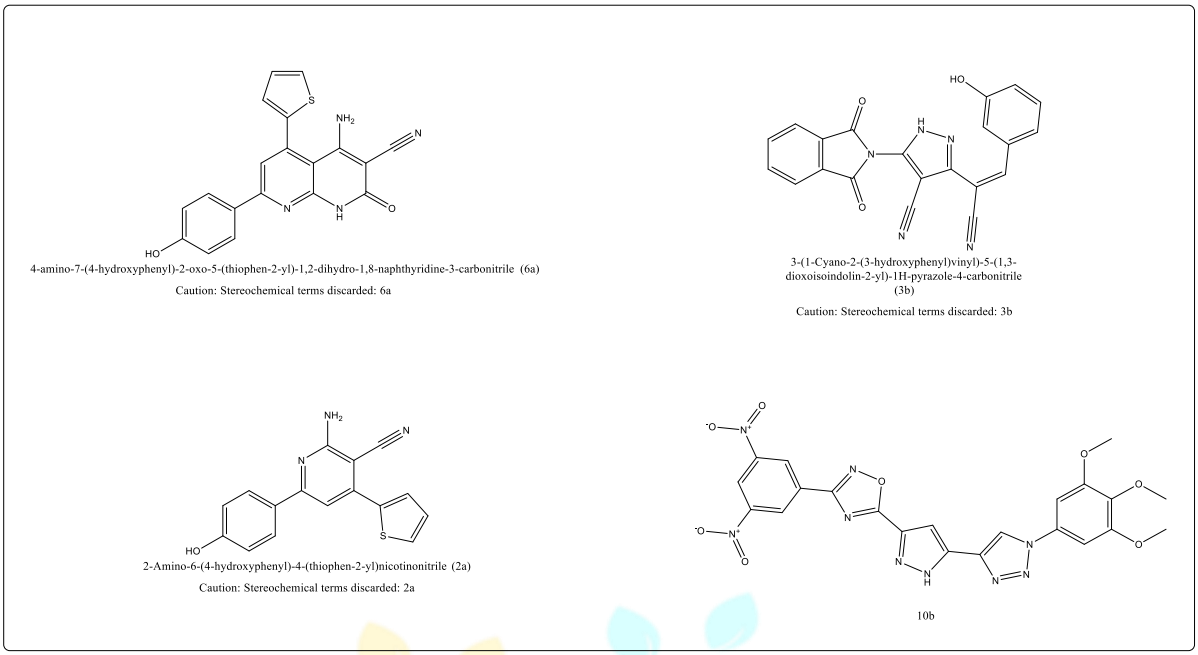
- Anticancer
- Anti-microbial
- Analgesic
- Anti-inflamatory etc.

Against human breast cancer cell line(MCF-7) pyrazole nepthalene derivatives (5a-5q) have tendency to treat and cure from braest cancer. (4) In anticancer agent, hybrid compounds have been synthesized by coupling thiazolidinone and pyrazole scaffolds. The most potent based on a docking (−9.307) and binding scores (−66.46) is 2-(1,3-diphenyl-1H-pyrazol-4-yl)-3-phenyl thiazolidin-4-one (4a) with good ADME parameters. 4a shows a maximum inhibition against lung cancer cell lines with a moderate inhibition rate of 31.01%. 4a having pyrazole-thiazolidinone ring systems and it is developed as anticancer agent. (5) The newly synthesized hybrid compounds pyrazole-isoxazole (4a-l) and pyrazole-1,2,3- triazole (5a-c) were evaluated for their cytotoxic activity against four human cancer cells. Hybrid compounds (4a-d) have the ability to treat very low anticancer activity (IC50 ≥ 100 μM) against the selected cells. With the combination of pyrazole and 1,2 ,3-triazole nucleus caused average cytotoxic effect with an IC50 against HT-1080. (6) 2, 3b, and 7b are the compound which are tested for the prepared compound against MCF-7 and it shows expressive activity with IC50.The binding energy of 2 is -42.318 KCal/mol ,3b is -30.535 KCal/mol and 7b is -32896 KCal/mol. Against tumor growth 3b is effective inhibitor activity and against CDK2 enzyme inhibition 86 is protective against cancer agents.



1,2,4-oxadiazole, 1,2,3-triazole-pyrazoles are synthesized and tested for anticancer activities against lung cancer, prostate cancer, and breast cancer with the use of MIT. Compound 10show the most anticancer activity against lung cancer, prostate cancer, and breast cancer with IC50. (8). Pyrazole possesses all type of biological activities. 4a shows the maximum inhabitation against lung cancer (NCI – H23) cell line for In Vitro anticancer activity. Doxorubicin is used as a positive control against anticancer activity. (9) 2a, 6a, 7a, 10b, 15a, and 18a compounds are superior in to treat HepG-2 and MCF-7 cancer cell lines. 10b and 2a derivatives achieved dual EGFR/VEGFR-2 inhibition with IC50 value of 0.161 and 0.141 μM. (10)

In series of 5-alkylated selanyl-1H-pyrazole derivatives 3a-d, 6a-d, and 4-amino-5-substitutedselenolo[2,3-c]pyrazole (4a-d). This is based on substitution of selenium chlorine atom inchloro pyrazole carbonitrile compound reduction with sodium borohydride. Elemental and spectroscopic techniques (FT-IR, 1 H, 13 C NMR, and mass spectrometry) are used to confirm the structure. 4c and 6d exhibit the highest cytotoxicity against HepG2 cell line with PIC50, which value is 4.30 and 4.49 without showing any toxicity. (11)



(E)-3-(3-(4-(benzyloxy)phenyl)-1-phenyl-1H-pyrazol-4-yl)-1-phenylprop-2-en-1-one were

synthesise and designed, tubulin polymerization is effective against MCF-7 (breast cancer), SiHa (cervical cancer) andf PC-3 (prostate cancer) cell lines. The is tested positive for binding mode at colchicine-binding site of tubuline protein. All the conjugated compound exhibit excellent cytotoxicity with the value of IC 50 value of 2.13 ± 0.80 µM. HEK cells do not exhibit significant toxicity. (12) Morpholine-benzimidazole-pyrazole hybrids shows anticancer activity against MCF-7, PC3, and A549 was reported effective. Against all the cancer cell lines etoposide is most active. 8k display superior activity against all cancer cell lines. (13) Pyrrole contain biheterocyclic derivatives that synthesise from pyrrole-azole. pyrrole-pyrazolones, pyrrole-pyrazoles and pyrrole 1,3,4 oxadiazoles are synthesized using cyclization of pyrrolyl hydrazide-hydrazone in the presence of special reagent. NLO analysis and anticancer activity and evaluation of synthesised compound. The structure of pyrazole were confirmed by modern spectroscopic method. All the calculations are performed by density functional theory (DFT). 5a-b, 6a-6b, 7a-7b are used against microbes and antimicrobial activity, these compounds are evaluate for their antiproliferative against HCT-116 (colon), and HL-60 (leukemia) these are two human cancer cell lines. Against the types of two human cancer cell lines this compound shows cytotoxicity effect. (14) From traditional medicinal plant new derivatives lead compounds are isolated. Against a panel of cancer cell lines aloe-emodin (6a–6e) were synthesise and assumed. Aloe-emodin derivatives could be a potential drug for better treatment of breast cancer. Pyrazole is synthesise and evaluate against many biological activities. (15) In the synthesis of novel urea derivatives of pyrimidine pyrazole and it screened for their activity. Compound 3,5-dinitro and 3,4,5-trimethoxy is more potent cytotoxicity than standard etoposide. The molecular docking of 3,5-dinitro and 3,4,5-trimethoxy occupied at colchicine binding site and β-tubuline interface of x-rays crystals. (16) 32 asymmetric MACs fused with 1-aryl-1H-pyrazole (7a-10h) were synthesise and characterized to develop new curcumin analogues. In screening of cytotoxic activity, nine compounds exhibit potential growth. (17)

Pyrazole derivatives and their modification with polymer microsphere are potential anticancer agents. X-rays and theoretical calculation are derivatives to molecular and crystal structures of pyrazole. Divinylbenzene and glycidyl methacrylate are manufacture on the basis of pyrazole derivatives and cross-linked polymer microsphere. Against normal cell line modified microsphere has in vitro antiproliferative activity. They have great ability to inhibit the all cancer cell line. The highest antiproliferative shows better action against cancer. (18) (E)-3-(3-(4-(benzyloxy)phenyl)-1-phenyl-1H-pyrazol-4-yl)-1-phenylprop-2-en-1-one (5a-r) were synthesise by 1 H, 13 C NMR, and ESI-MS and evaluate tubulin polymerization and

invitro cytotoxicity against MCF7, SiHa, and PC3 as well as HEK-293T cancer cell lines. At the site of tubulin binding mode at colchicine- binding. All the synthesised conjugated exhibit cyctotoxicity with IC 50 value of 2.13 ± 0.80 µM (MCF-7), 4.34 ± 0.98 µM (SiHa), and 4.46 ± 0.53 µM (PC-3) against cancer cell lines. (19) In the reaction of 3-aminopyrazoles with dimethylamino-acrylonitrile derivatives are utilize for the production of new functionalized pyrazolopyrimidine compound (4a-c) and (6a-c). The investigated derivatives exhibit HOMO LUMO energy gap ranging from 2.70 to 2.34Ev. The anticancer activities of synthesise compound have been investigated against four cancer cells. (20)

Conclusion:

References:

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